

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L8	586	I7 and bone and cement	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/09/19 18:11
L9	29	I7 and bone and cement and substitute and osteomyelitis	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/09/19 18:18
L10	29	I7 and bone and cement and substitute and osteomyelitis and (antimicrobial or antibiotic or antiseptic)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/09/19 18:20
L11	8	I7.clm. and bone and cement and substitute and osteomyelitis and (antimicrobial or antibiotic or antiseptic)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/09/19 18:20

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NEWS 2 "Ask CAS" for self-help around the clock  
NEWS 3 FEB 27 New STN AnaVist pricing effective March 1, 2006  
NEWS 4 MAY 10 CA/CAPLUS enhanced with 1900-1906 U.S. patent records  
NEWS 5 MAY 11 KOREAPAT updates resume  
NEWS 6 MAY 19 Derwent World Patents Index to be reloaded and enhanced  
NEWS 7 MAY 30 IPC 8 Rolled-up Core codes added to CA/CAPLUS and  
USPATFULL/USPAT2  
NEWS 8 MAY 30 The F-Term thesaurus is now available in CA/CAPLUS  
NEWS 9 JUN 02 The first reclassification of IPC codes now complete in  
INPADOC  
NEWS 10 JUN 26 TULSA/TULSA2 reloaded and enhanced with new search and  
and display fields  
NEWS 11 JUN 28 Price changes in full-text patent databases EPFULL and PCTFULL  
NEWS 12 JUL 11 CHEMSAFE reloaded and enhanced  
NEWS 13 JUL 14 FSTA enhanced with Japanese patents  
NEWS 14 JUL 19 Coverage of Research Disclosure reinstated in DWPI  
NEWS 15 AUG 09 INSPEC enhanced with 1898-1968 archive  
NEWS 16 AUG 28 ADISCTI Reloaded and Enhanced  
NEWS 17 AUG 30 CA(SM)/CAPLUS(SM) Austrian patent law changes  
NEWS 18 SEP 11 CA/CAPLUS enhanced with more pre-1907 records  
  
NEWS EXPRESS. JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT  
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.  
  
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NEWS LOGIN Welcome Banner and News Items  
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FILE 'HOME' ENTERED AT 17:27:19 ON 19 SEP 2006

=> file registry  
COST IN U.S. DOLLARS  
FULL ESTIMATED COST

SINCE FILE	TOTAL
ENTRY	SESSION
0.21	0.21

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STRUCTURE FILE UPDATES: 18 SEP 2006 HIGHEST RN 907539-37-1  
DICTIONARY FILE UPDATES: 18 SEP 2006 HIGHEST RN 907539-37-1

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<http://www.cas.org/ONLINE/UG/regprops.html>

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=> LLLFLLKKRKKRKY/SQEP
      1 LLLFLLKKRKKRKY/SQEP
      57753 SQL=14
L1      1 LLLFLLKKRKKRKY/SQEP
      (LLLFLLKKRKKRKY/SQEP AND SQL=14)
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=> d 11 sqd 1

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L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 230974-92-2 REGISTRY
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 14.
```

PATENT ANNOTATIONS (PNTE):

Sequence	Patent
Source	Reference
=====+	=====
Not Given	WO2000001427
	claimed PAGE
	13

```
SEQ      1 LLLFLLKKRK KRKY
      =====
HITS AT: 1-14
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      2 KRKFHEKHHSRGGY/SQEP
      57753 SQL=14
L2      2 KRKFHEKHHSRGGY/SQEP
      (KRKFHEKHHSRGGY/SQEP AND SQL=14)
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=> d 11 sqd 1-2

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L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
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RN 230974-92-2 REGISTRY  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL 14

PATENT ANNOTATIONS (PNTE):

Sequence |Patent  
Source |Reference  
=====+=====

Not Given	WO2000001427
	claimed PAGE
	13

SEQ 1 LLLFLLKKRK KRKY  
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HITS AT: 1-14

=> d 12 sqd 1-2

L2 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 274251-24-0 REGISTRY  
FS PROTEIN SEQUENCE  
SQL 29,15,14  
NTE multichain  
modified

type	-----	location	-----	description
terminal mod.	Lys-15	-		C-terminal amide
bridge	Lys-15	- Tyr-14'		amide bridge

SEQ 1 KRKFHEKHHS HRGYK  
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HITS AT: 1-14

SEQ 1 KRKFHEKHHS HRGY  
=====

HITS AT: 1-14

L2 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 155113-11-4 REGISTRY  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL 14

PATENT ANNOTATIONS (PNTE):

Sequence |Patent  
Source |Reference  
=====+=====

Not Given	EP1228772
	claimed
	SEQID 1

SEQ 1 KRKFHEKHHS HRGY  
=====

HITS AT: 1-14

=> KRLFKKLKFSLRKY

L3 0 KRLFKKLKFSLRKY  
0 KRLFKKLKFSLRKY

=> KRLFKKLKFSLRKY/sqe

SEQUENCE QUALIFICATION '/SQE' IS NOT VALID

2 KRLFKKCLKFSLRKY/SQEP  
57753 SQL=14

L4 2 KRLFKKCLKFSLRKY/SQEP  
(KRLFKKCLKFSLRKY/SQEP AND SQL=14)

The field code specified is no longer in use. Enter "HELP SFIELDS"  
at an arrow prompt (=>) to see a list of valid field codes.

=> KRLFKKCLKFSLRKY/sqep  
2 KRLFKKCLKFSLRKY/SQEP  
57753 SQL=14  
L5 2 KRLFKKCLKFSLRKY/SQEP  
(KRLFKKCLKFSLRKY/SQEP AND SQL=14)

=> d 13 sqd 1-2  
L3 HAS NO ANSWERS  
L3 0 SEA FILE=REGISTRY PLU=ON KRLFKKCLKFSLRKY

=> d 15 sqd 1-2

L5 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 274251-39-7 REGISTRY  
FS PROTEIN SEQUENCE  
SQL 29,15,14  
NTE multichain  
modified

type	location	description
terminal mod.	Lys-15	- C-terminal amide
bridge	Lys-15	- Tyr-14' amide bridge

SEQ 1 KRLFKKCLKFS LRKY  
=====

HITS AT: 1-14

SEQ 1 KRLFKKCLKFS LRKY  
=====

HITS AT: 1-14

L5 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 230974-91-1 REGISTRY  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL 14

PATENT ANNOTATIONS (PNTE):  
Sequence |Patent  
Source |Reference  
=====+=====

Not Given	WO2000001427
	claimed PAGE
	11

SEQ 1 KRLFKKCLKFS LRKY  
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HITS AT: 1-14

=>  
=>  
=> FKCRWQWRMKKLG/sqed  
'SQED' IS NOT A VALID FIELD CODE

L6 0 FKCRRWQWRMKKLG/SQED

=> FKCRRWQWRMKKLG/sqep

1 FKCRRWQWRMKKLG/SQEP  
57753 SQL=14

L7 1 FKCRRWQWRMKKLG/SQEP  
(FKCRRWQWRMKKLG/SQEP AND SQL=14)

=> d 17 sqd 1-2

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 252209-80-6 REGISTRY  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL 14

PATENT ANNOTATIONS (PNTE):

Sequence |Patent

Source |Reference

=====+=====

Not Given|EP1228772

|claimed

|SEQID 5

SEQ 1 FKCRRWQWRM KKLK

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HITS AT: 1-14

=> GRRRRSVQWCA/SQEP

4 GRRRRSVQWCA/SQEP  
89236 SQL=11

L8 4 GRRRRSVQWCA/SQEP  
(GRRRRSVQWCA/SQEP AND SQL=11)

=> d 18 sqd 1-4

L8 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 191113-83-4 REGISTRY  
FS PROTEIN SEQUENCE  
SQL 47,36,11  
NTE multichain

type	-----	location	-----	description
bridge	Cys-9	- Cys-26		disulfide bridge
bridge	Cys-35	- Cys-10'		disulfide bridge

SEQ 1 VSQPEATKCF QTQRNMRKVR GPPVSCIKRD SPIQCI

SEQ 1 GRRRRSVQWC A

=====

HITS AT: 1-11

L8 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 183623-03-2 REGISTRY  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL 11

PATENT ANNOTATIONS (PNTE):

Sequence |Patent

Source |Reference

=====+=====

Not Given|WO2001034641

|claimed  
|SEQID 2

SEQ 1 GRRRRSVQWC A

=====

HITS AT: 1-11

L8 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 172520-63-7 REGISTRY  
FS PROTEIN SEQUENCE  
SQL 47,36,11  
NTE multichain

type	location	description
bridge	Cys-9 - Cys-26	disulfide bridge
bridge	Cys-35 - Cys-10'	disulfide bridge

SEQ 1 VSQPEATKCF QWQRNMRKVR GPPVSCIKRD SPIQCI

SEQ 1 GRRRRSVQWC A

=====

HITS AT: 1-11

\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

L8 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 142461-97-0 REGISTRY  
DR 170904-94-6, 176086-93-4  
FS PROTEIN SEQUENCE  
SQL 47,36,11  
NTE multichain

type	location	description
bridge	Cys-9 - Cys-26	disulfide bridge
bridge	Cys-35 - Cys-10'	disulfide bridge

SEQ 1 VSQPEATKCF QWQRNMRKVR GPPVSCIKRD SPIQCI

SEQ 1 GRRRRSVQWC A

=====

HITS AT: 1-11

\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

=> SSSKEENRIIPGGI/SQEP  
1 SSSKEENRIIPGGI/SQEP  
57753 SQL=14  
L9 1 SSSKEENRIIPGGI/SQEP  
(SSSKEENRIIPGGI/SQEP AND SQL=14)

=> d 19 sqd 1-4

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 220126-74-9 REGISTRY  
FS PROTEIN SEQUENCE; STEREOSEARCH  
SQL 14

PATENT ANNOTATIONS (PNTE):  
Sequence |Patent

Source |Reference  
=====+=====  
Not Given|EP1228772  
|claimed  
|SEQID 7

SEQ 1 SSSKEENRII PGGI  
=====

HITS AT: 1-14

=> file caplus medline embase biosis  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
115.99	116.20

FILE 'CAPLUS' ENTERED AT 17:38:59 ON 19 SEP 2006  
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FILE 'REGISTRY' ENTERED AT 17:27:40 ON 19 SEP 2006

L1	1 LLLFLLKKRKKRKY/SQEP
L2	2 KRKFHEKHSHRGY/SQEP
L3	0 KRLFKKLKFSRLKY
L4	2 KRLFKKLKFSRLKY/SQE
L5	2 KRLFKKLKFSRLKY/SQEP
L6	0 FKCRWQWRMCKLG/SQED
L7	1 FKCRWQWRMCKLG/SQEP
L8	4 GRRRSVQWCA/SQEP
L9	1 SSSKEENRIIPGGI/SQEP

FILE 'CAPLUS, MEDLINE, EMBASE, BIOSIS' ENTERED AT 17:38:59 ON 19 SEP 2006

=> 11 or 12 or 15 or 17 or 18 or 19

L10 69 L1 OR L2 OR L5 OR L7 OR L8 OR L9

=> dup rem l10

PROCESSING COMPLETED FOR L10

L11 63 DUP REM L10 (6 DUPLICATES REMOVED)

=> d ibib abs total

L11 ANSWER 1 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:239120 CAPLUS

DOCUMENT NUMBER: 142:292527

TITLE: Recombinant expression of antimicrobial agents and  
enzymes through a cleavable linker, and applications  
for animal feed and animal feed additives

INVENTOR(S): Jensen, Ejner Bech; Hogenhaug, Hans-Henrik Kristensen;  
Hansen, Peter Kamp; Pedersen, Poul Erik; Mygind, Per  
Holse



PATENT ASSIGNEE(S): Novozymes A/S, Den.  
 SOURCE: PCT Int. Appl., 102 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005024002	A1	20050317	WO 2004-DK605	20040913
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

AU 2004270815	A1	20050317	AU 2004-270815	20040913
CA 2536782	AA	20050317	CA 2004-2536782	20040913
EP 1680503	A1	20060719	EP 2004-762825	20040913

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

PRIORITY APPLN. INFO.: DK 2003-1310 A 20030911  
 WO 2004-DK605 W 20040913

AB The current invention provides recombinant expression of antimicrobial agents and enzymes, in particular co-expression of antimicrobial peptide with an enzyme through a cleavable linker. Examples of antimicrobial agents are antimicrobial peptides such as lactoferricins and antimicrobial enzymes such as lysozyme and glucose oxidase, and examples of enzymes are endoglucanase, xylanase, phytase, protease, galactanase, mannanase, dextranase,  $\alpha$ -galactosidase, pectate lyase,  $\alpha$ -amylase and glucoamylase. The products can be used in animal feed and animal feed additives.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2005:384782 CAPLUS

DOCUMENT NUMBER: 143:353214

TITLE: The effect of the antimicrobial peptide, Dhvar-5, on gentamicin release from a polymethyl methacrylate bone cement

AUTHOR(S): Faber, C.; Hoogendoorn, R. J. W.; Lyaruu, D. M.; Stallmann, H. P.; van Marle, J.; van Nieuw Amerongen, A.; Smit, T. H.; Wuisman, P. I. J. M.

CORPORATE SOURCE: SKELETAL TISSUE ENGINEERING GROUP AMSTERDAM, Department of Orthopaedic Surgery, VU University Medical Center (VUmc), Vrije Universiteit, Amsterdam, 1007 MB, Neth.

SOURCE: Biomaterials (2005), 26(28), 5717-5726  
 CODEN: BIMADU; ISSN: 0142-9612

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The objective of this study was to investigate the release mechanism and kinetics of the antimicrobial peptide, Dhvar-5, both alone and in combination with gentamicin, from a standard com. polymethyl methacrylate (PMMA) bone cement. Different amts. of Dhvar-5 were mixed with the bone cement powders of Osteopal and the gentamicin-containing Osteopal G bone cement and their release kinetics from the polymerized cement were

investigated. Addnl., the internal structure of the bone cements were analyzed by SEM (SEM) of the fracture surfaces. Secondly, porosity was investigated with the mercury intrusion method and related to the observed release profiles. In order to obtain an insight into the mech. characteristics of the bone cement mixts., the compressive strength of Osteopal and Osteopal G with Dhvar-5 was also investigated. The total Dhvar-5 release reached 96% in the 100 mg Dhvar-5/g Osteopal cement, whereas total gentamicin release from Osteopal G reached only 18%. Total gentamicin release increased significantly to 67% with the addition of 50 mg Dhvar-5/g, but the Dhvar-5 release was not influenced. SEM showed an increase of dissolved gentamicin crystals with the addition of Dhvar-5. The mercury intrusion results suggested an increase of small pores (<0.1  $\mu\text{m}$ ) with the addition of Dhvar-5. Compressive strength of Osteopal was reduced by the addition of Dhvar-5 and gentamicin, but still remained above the limit prescribed by the ISO standard for clin. bone cements. We therefore conclude that the antimicrobial peptide, Dhvar-5, was released in high amts. from PMMA bone cement. When used together with gentamicin sulfate, Dhvar-5 made the gentamicin crystals accessible for the release medium presumably through increased micro-porosity (<0.1  $\mu\text{m}$ ) resulting in a fourfold increase of gentamicin release.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1253417 CAPLUS

DOCUMENT NUMBER: 144:100422

TITLE: Histatin and lactoferrin derived peptides:  
Antimicrobial properties and effects on mammalian cells

AUTHOR(S): Stallmann, Hein P.; Faber, Chris; Bronckers, Antonius L. J. J.; de Blicke-Hogervorst, Jolanda M. A.; Brouwer, Carlo P. J. M.; Nieuw Amerongen, Arie V.; Wuisman, Paul I. J. M.

CORPORATE SOURCE: Orthopedic Surgery, VU Medical Center, Amsterdam, 1007 MB, Neth.

SOURCE: Peptides (New York, NY, United States) (2005), 26(12), 2355-2359

CODEN: PPTDD5; ISSN: 0196-9781

PUBLISHER: Elsevier Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In order to analyze the clin. potential of two antimicrobial peptides, human lactoferrin 1-11 (hLF1-11) and synthetic histatin analog Dhvar-5, the authors measured the killing effect on bacteria, and the potential toxicity on erythrocytes and bone cells. The antimicrobial activity was determined in a killing assay on six strains, including methicillin resistant *Staphylococcus Aureus*. The effect on human erythrocytes and MC3T3 mouse bone cells was measured with a hemolysis assay and a viability assay, resp. Both hLF1-11 and Dhvar-5 dose-dependently killed all bacterial strains, starting at concns. of 6  $\mu\text{g/mL}$ . HLF1-11 had no effect on mammalian cells at concns. up to 400  $\mu\text{g/mL}$ , but Dhvar-5 induced significant hemolysis (37% at 200  $\mu\text{g/mL}$ ) and bone cell death (70% at 400  $\mu\text{g/mL}$ ). This indicates that both peptides are able to kill various resistant and nonresistant bacteria, but Dhvar-5 may exert a cytotoxic effect on host cells at higher concns.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:473422 CAPLUS

DOCUMENT NUMBER: 141:34653

TITLE: Expression of human milk proteins in transgenic plants

INVENTOR(S): Huang, Ning; Rodriguez, Raymond L.; Hagie, Frank E.

PATENT ASSIGNEE(S): Ventria Bioscience, USA

SOURCE: U.S. Pat. Appl. Publ., 111 pp., Cont.-in-part of U.S.

Pat. Appl. 2003 74,700.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

10

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004111766	A1	20040610	US 2003-639835	20030812
US 2003172403	A1	20030911	US 2001-847232	20010502
US 2003074700	A1	20030417	US 2002-77381	20020214
US 6991824	B2	20060131		
CA 2525493	AA	20041118	CA 2003-2525493	20030411
AU 2003218396	A1	20041126	AU 2003-218396	20030411
EP 1651760	A1	20060503	EP 2003-714394	20030411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK				
WO 2005017168	A1	20050224	WO 2004-US26230	20040812
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, US				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005229273	A1	20051013	US 2005-83617	20050316
PRIORITY APPLN. INFO.:			US 2000-201182P	P 20000502
			US 2001-266920P	P 20010206
			US 2001-269199P	P 20010214
			US 2001-847232	A2 20010502
			US 2002-77381	A2 20020214
			WO 2003-US9209	W 20030411
			US 2003-639835	A 20030812

AB The invention is directed to seed and seed extract compns. containing levels of a

human milk protein between 3-40% or higher of the total protein weight of the soluble protein extractable from the seed. Also disclosed is a method of producing the seed with high levels of extractable human milk protein. The method includes transforming a monocotyledonous plant with a chimeric gene having a protein-coding sequence encoding a protein normally present in human milk under the control of a seed maturation-specific promoter. The method may further includes a leader DNA sequence encoding a monocot seed-specific transit sequence capable to target a linked milk protein to a storage body.

L11 ANSWER 5 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:1058364 CAPLUS

DOCUMENT NUMBER:

142:43768

TITLE:

Protease inhibitors containing lactoferrin and transferrin-derived peptides

INVENTOR(S):

Katsunuma, Nobuhiko

PATENT ASSIGNEE(S):

Morinaga Milk Industry Co., Ltd., Japan

SOURCE:

Jpn. Kokai Tokkyo Koho, 36 pp.

CODEN: JKXXAF

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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-----  
JP 2004346020      A2      20041209      JP 2003-145457      20030522  
PRIORITY APPLN. INFO.:      JP 2003-145457      20030522

AB The invention relates to a cysteine protease inhibitor characterized by containing lactoferrin, transferrin and/or their partial peptide as an active component, suitable for use in a pharmaceutical, food, or feed composition for prevention and/or treatment of osteoporosis and neoplastic hypercalcemia. The effects of cattle lactoferrin on papain, cathepsin B, cathepsin L, and cathepsin S activities were in vitro tested. Also, a tablet containing cattle lactoferrin 40 % was formulated.

L11 ANSWER 6 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1056181 CAPLUS

DOCUMENT NUMBER: 143:284329

TITLE: PspA protects *Streptococcus pneumoniae* from killing by apolactoferrin, and antibody to PspA enhances killing of pneumococci by apolactoferrin. [Erratum to document cited in CA141:312601]

AUTHOR(S): Shaper, Mirza; Hollingshead, Susan K.; Benjamin, William H., Jr.; Briles, David E.

CORPORATE SOURCE: Department of Microbiology, University of Alabama at Birmingham, Birmingham, AL, USA

SOURCE: Infection and Immunity (2004), 72(12), 7379

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The corrected byline is given. The author list is Shaper Mirza, Susan K. Hollingshead, William H. Benjamin, Jr., and David E. Briles. Shaper Mirza, Susan K. Hollingshead, and David E. Briles are affiliated with the Department of Microbiol., and William H. Benjamin, Jr., with the Department of Pathol., University of Alabama at Birmingham, Birmingham, Alabama.

L11 ANSWER 7 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:724191 CAPLUS

DOCUMENT NUMBER: 141:312601

TITLE: PspA protects *Streptococcus pneumoniae* from killing by apolactoferrin, and antibody to PspA enhances killing of pneumococci by apolactoferrin

AUTHOR(S): Shaper, Mirza; Hollingshead, Susan K.; Benjamin, William H., Jr.; Briles, David E.

CORPORATE SOURCE: Department of Microbiology, University of Alabama at Birmingham, Birmingham, AL, USA

SOURCE: Infection and Immunity (2004), 72(9), 5031-5040

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lactoferrin is an important component of innate immunity through its sequestration of iron, bactericidal activity, and immune modulatory activity. Apolactoferrin (ALF) is the iron-depleted form of lactoferrin and is bactericidal against pneumococci and several other species of bacteria. We observed that lactoferricin (LFN), an 11-amino-acid peptide from the N terminus of lactoferrin, is bactericidal for *Streptococcus pneumoniae*. Strains of *S. pneumoniae* varied in their susceptibility to ALF. Lactoferrin is bound to the pneumococcal surface by pneumococcal surface protein A (PspA). Using mutant PspA- pneumococci of four different strains, we observed that PspA offers significant protection against killing by ALF. Knockout mutations in genes for two other choline-binding proteins (PspC and PcpA) did not affect killing by ALF. PspA did not have to be attached to the bacterial surface to inhibit killing, because the soluble recombinant N-terminal half of PspA could prevent killing by both ALF and LFN. An 11-amino-acid fragment of PspA was also able to reduce the killing by LFN. Antibody to PspA enhanced

killing by lactoferrin. These findings suggested that the binding of ALF to PspA probably blocks the active site(s) of ALF that is responsible for killing.

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2004:1070044 CAPLUS

DOCUMENT NUMBER: 142:169087

TITLE: In vivo comparison of Dhvar-5 and gentamicin in an MRSA osteomyelitis prevention model

AUTHOR(S): Faber, Christopher; Hoogendoorn, Roel J. W.; Stallmann, Hein P.; Lyaruu, D. M.; van Nieuw Amerongen, Arie; Wuisman, Paul I. J. M.

CORPORATE SOURCE: Department of Orthopaedic Surgery, VU University Medical Center, Amsterdam, 1007 MB, Neth.

SOURCE: Journal of Antimicrobial Chemotherapy (2004), 54(6), 1078-1084

CODEN: JACHDX; ISSN: 0305-7453

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The continued rise in drug-resistant pathogens has led to global research efforts into new antimicrobial agents. A promising class of new agents are the antimicrobial peptides. The aim of the study was to investigate the efficacy of the antimicrobial peptide Dhvar-5 in a prophylactic, methicillin-resistant *Staphylococcus aureus* (MRSA) osteomyelitis model. Dhvar-5 (12 mg or 24 mg/rabbit) was incorporated into polymethyl methacrylate (PMMA) beads as a local drug delivery system. For comparison, plain beads (control) and beads containing gentamicin as a sulfate (10 mg or 24 mg per rabbit) were also prepared. The beads were inserted into the inoculated femoral cavity of 36 rabbits, and 1 wk later they were killed. The presence and severity of MRSA osteomyelitis was assessed by culture and histol. Both the 24 mg Dhvar-5 beads and the 24 mg gentamicin sulfate beads significantly reduced the bacterial load of the inoculated femora compared with the control chain. Although a 24 mg Dhvar-5 dose inhibited MRSA growth, it did not completely sterilize the femora. Sterilization occurred only in some of the gentamicin-treated specimens. The authors conclude that both the gentamicin beads and the Dhvar-5 beads were only partially effective at preventing MRSA infection in this model.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:350531 CAPLUS

DOCUMENT NUMBER: 141:101810

TITLE: Interactions of histatin 5 and histatin 5-derived peptides with liposome membranes: surface effects, translocation and permeabilization

AUTHOR(S): denHertog, Alice L.; Sang, Harro W. Wong Fong; Kraayenhof, Ruud; Bolscher, Jan G. M.; Van't Hof, Wim; Veerman, Enno C. I.; Nieuw Amerongen, Arie V.

CORPORATE SOURCE: Academic Centre for Dentistry Amsterdam (ACTA), Section Oral Biochemistry, Department of Dental Basic Sciences, Vrije Universiteit, Amsterdam, 1081 BT, Neth.

SOURCE: Biochemical Journal (2004), 379(3), 665-672

CODEN: BIJOAK; ISSN: 0264-6021

PUBLISHER: Portland Press Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A number of cationic antimicrobial peptides, among which are histatin 5 and the derived peptides dhvar4 and dhvar5, enter their target cells and interact with internal organelles. There still are questions about the mechanisms by which antimicrobial peptides translocate across the

membrane. We used a liposome model to study membrane binding, translocation and membrane-perturbing capacities of histatin 5, dhvar4 and dhvar5. Despite the differences in amphipathic characters of these peptides, they bound equally well to liposomes, whereas their membrane activities differed remarkably: dhvar4 translocated at the fastest rate, followed by dhvar5, whereas the histatin 5 translocation rate was much lower. The same pattern was seen for the extent of calcein release: highest with dhvar4, less with dhvar5 and almost none with histatin 5. The translocation and disruptive actions of dhvar5 did not seem to be coupled, because translocation occurred on a much longer timescale than calcein release, which ended within a few minutes. We conclude that peptide translocation can occur through peptide-phospholipid interactions, and that this is a possible mechanism by which antimicrobial peptides enter cells. However, the translocation rate was much lower in this model membrane system than that seen in yeast cells. Thus it is likely that, at least for some peptides, addnl. features promoting the translocation across biol. membranes are involved as well.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:748239 CAPLUS

DOCUMENT NUMBER: 142:19776

TITLE: Release of calcium from intracellular stores and subsequent uptake by mitochondria are essential for the candidacidal activity of an N-terminal peptide of human lactoferrin

AUTHOR(S): Lupetti, Antonella; Brouwer, Carlo P. J. M.; Dogterom-Ballering, Heleen E. C.; Senesi, Sonia; Campa, Mario; van Dissel, Jaap T.; Nibbering, Peter H.  
CORPORATE SOURCE: Department of Infectious Diseases, Leiden University Medical Center (LUMC), Leiden, 2300 RC, Neth.

SOURCE: Journal of Antimicrobial Chemotherapy (2004), 54(3), 603-608

CODEN: JACHDX; ISSN: 0305-7453

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Earlier studies showed that mitochondrial damage is a hallmark of the candidacidal activity of an N-terminal peptide of human lactoferrin, further referred to as hLF(1-11). Since uptake of Ca<sup>2+</sup> by mitochondria may be essential for their activation, the aim of this study was to define the role of Ca<sup>2+</sup> in killing of *Candida albicans* by the hLF(1-11) peptide. The effect of compds. interfering with Ca<sup>2+</sup> homeostasis on the hLF(1-11)-induced candidacidal activity, changes in mitochondrial membrane potential, and reactive oxygen species production were evaluated using a killing assay, rhodamine 123 staining, and 2',7'-dichlorofluorescein diacetate, resp. The increase in cellular Ca<sup>2+</sup> content was measured using 45Ca<sup>2+</sup>. Our results revealed that Ruthenium Red, which inhibits the mitochondrial Ca<sup>2+</sup>-uniporter and the voltage-sensitive Ca<sup>2+</sup> release from internal stores, blocked (P<0.05) the hLF(1-11)-induced candidacidal activity as well as changes in the membrane potential of mitochondria, and reactive oxygen species production. Oxalate, which ppts. Ca<sup>2+</sup> in intracellular organelles, decreased (P<0.05) the peptide-induced changes in the membrane potential of mitochondria, reactive oxygen species production, and candidacidal activity. Furthermore, the Ca<sup>2+</sup> ionophore ionomycin combined with high CaCl<sub>2</sub> concns. enhanced the hLF(1-11)-induced candidacidal activity. Moreover, hLF(1-11) caused an influx of Ca<sup>2+</sup> from the extracellular medium into *C. albicans* reaching a three-fold increase at 2 h, whereas no increase was found in unexposed cells. In agreement, the Ca<sup>2+</sup>-chelator EGTA blocked the peptide-induced candidacidal activity. Thus, Ca<sup>2+</sup> release from intracellular stores, probably through subsequent mitochondrial Ca<sup>2+</sup> uptake, is essential for the hLF(1-11)-induced candidacidal activity.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:721139 CAPLUS

DOCUMENT NUMBER: 141:235763

TITLE: Osteomyelitis prevention in rabbits using antimicrobial peptide hLF1-11- or gentamicin-containing calcium phosphate cement

AUTHOR(S): Stallmann, Hein P.; Faber, Christopher; Bronckers, Antonius L. J. J.; Nieuw Amerongen, Arie V.; Wuisman, Paul I. J. M.

CORPORATE SOURCE: Department of Orthopaedic Surgery, VU University Medical Center, Amsterdam, 1007 MB, Neth.

SOURCE: Journal of Antimicrobial Chemotherapy (2004), 54(2), 472-476

CODEN: JACHDX; ISSN: 0305-7453

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The efficacy of prophylactic treatment with human lactoferrin 1-11 (hLF1-11), a broad-spectrum antimicrobial peptide, was studied in a rabbit model of femur infection. Calcium phosphate cement with 50 mg/g hLF1-11 or gentamicin was injected into the femoral canal, after inoculation with *Staphylococcus aureus*. Three weeks later, slices of the proximal femora were sawn for quant. bacterial culture and histol. Treatment with hLF1-11 ( $P < 0.038$ ) or gentamicin ( $P < 0.008$ ) caused a reduction of cfu compared with the untreated control rabbits. The number of sterile cultures was higher in hLF1-11- (3/7) and gentamicin- (5/6) treated animals than in controls (1/7). Radiol. and histol. anal. showed early bone ingrowth into the cement cracks, and only moderate pathol. changes in rabbits with pos. cultures. Local prophylaxis with hLF1-11 effectively reduced development of osteomyelitis in a rabbit model, but gentamicin resulted in a larger number of sterile femora.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:204874 CAPLUS

DOCUMENT NUMBER: 141:345721

TITLE: <sup>99m</sup>Tc-labeled UBI 29-41 peptide for monitoring the efficacy of antibacterial agents in mice infected with *Staphylococcus aureus*

AUTHOR(S): Nibbering, Peter H.; Welling, Mick M.; Paulusma-Annema, Akke; Brouwer, Carlo P. J. M.; Lupetti, Antonella; Pauwels, Ernest K. J.

CORPORATE SOURCE: Department of Infectious Diseases, Leiden University Medical Center, Leiden, 2300 RC, Neth.

SOURCE: Journal of Nuclear Medicine (2004), 45(2), 321-326

CODEN: JNMEAQ; ISSN: 0161-5505

PUBLISHER: Society of Nuclear Medicine

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Based on our earlier observation that <sup>99m</sup>Tc-UBI 29-41, a radiolabeled peptide derived from ubiquicidin (UBI), discriminates between infections and sterile inflammatory processes, we considered the possibility that this tracer could be used for monitoring the efficacy of antibacterial agents in animals infected with *Staphylococcus aureus*. Methods: We injected <sup>99m</sup>Tc-UBI 29-41 into *S. aureus*-infected mice after treatment with various doses of cloxacillin or erythromycin. At intervals thereafter, accumulation of the radiolabeled peptide at the site of infection was assessed by scintigraphy. When *S. aureus* was antibiotic resistant, we evaluated the efficacy of hLF 1-11, an antimicrobial peptide derived from human lactoferrin (hLF), in rats using <sup>99m</sup>Tc-UBI 29-41 and scintigraphy. Results: Decreasing amts. of radiolabeled peptide at the site of the *S. aureus* infection in animals correlated ( $r^2 > 0.81$ ;  $P < 0.001$ ) with

increasing doses of cloxacillin in animals. An ED of erythromycin resulted in reduced ( $P = 0.023$ ) accumulation of the radiolabeled peptide at the site of *S. aureus* infection in mice. In addition, we noted decreasing amts. of <sup>99m</sup>Tc-UBI 29-41 at the site of infection after administration of increasing doses of hLF 1-11 peptide in rats infected with antibiotic-resistant *S. aureus*. Furthermore, the number of viable bacteria decreased with increasing doses of cloxacillin or hLF 1-11 peptide, and a good correlation ( $r^2 > 0.80$ ;  $P < 0.001$ ) between the accumulation of <sup>99m</sup>Tc-UBI 29-41 and the number of viable (antibiotic-resistant) *S. aureus* at the site of infection was seen. In an attempt to explain these results, we found that these antibacterial agents do not affect the in vitro binding of <sup>99m</sup>Tc-UBI 29-41 to bacteria. Furthermore, this radiolabeled peptide bound to free bacteria and to cell-adherent but not phagocytized *S. aureus*, suggesting that at sites of infection mainly extracellular bacteria are targeted by <sup>99m</sup>Tc-UBI 29-41. Conclusion: <sup>99m</sup>Tc-UBI 29-41 allows the monitoring of the efficacy of antibacterial agents in mice and rats with *S. aureus* infections.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:279792 CAPLUS

DOCUMENT NUMBER: 141:33358

TITLE: Lactoferrampin: a novel antimicrobial peptide in the N1-domain of bovine lactoferrin

AUTHOR(S): van der Kraan, Marieke I. A.; Groenink, Jasper; Nazmi, Kamran; Veerman, Enno C. I.; Bolscher, Jan G. M.; Nieuw Amerongen, Arie V.

CORPORATE SOURCE: Department of Oral Biochemistry, Academic Centre for Dentistry Amsterdam (ACTA), Amsterdam, 1081 BT, Neth. Peptides (New York, NY, United States) (2004), 25(2), 177-183

SOURCE: CODEN: PPTDD5; ISSN: 0196-9781

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The antimicrobial activity of bovine lactoferrin is attributed to lactoferricin, situated in the N1-domain. Based on common features of antimicrobial peptides, a second putative antimicrobial domain was identified in the N1-domain of lactoferrin, designated lactoferrampin. This novel peptide exhibited candidacidal activity, which was substantially higher than the activity of lactoferrin. Furthermore, lactoferrampin was active against *Bacillus subtilis*, *Escherichia coli*, and *Pseudomonas aeruginosa*, but not against the fermenting bacteria *Actinomyces naeslundii*, *Porphyromonas gingivalis*, *Streptococcus mutans* and *Streptococcus sanguis*. Notably, lactoferrampin is located in the N1-domain in close proximity to lactoferricin, which plays a crucial role in membrane-mediated activities of lactoferrin.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 63 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:324189 BIOSIS

DOCUMENT NUMBER: PREV200400324259

TITLE: Anti-complement effects of lactoferrin-derived peptides.

AUTHOR(S): Samuelsen, Orian [Reprint Author]; Haukland, Hanne H.; Ulvatne, Hilde; Vorland, Lars H.

CORPORATE SOURCE: Dept Med Microbiol, Univ Hosp N Norway, POB 56, N-9038, Tromso, Norway  
orjan.samuelsen@unn.no

SOURCE: FEMS Immunology and Medical Microbiology, (June 1 2004) Vol. 41, No. 2, pp. 141-148. print.  
ISSN: 0928-8244 (ISSN print).

DOCUMENT TYPE: Article



LANGUAGE: English  
ENTRY DATE: Entered STN: 21 Jul 2004  
Last Updated on STN: 21 Jul 2004

AB Lactoferrin is an important biological molecule with many functions such as modulation of the inflammatory response, iron metabolism and antimicrobial defense. One effect of lactoferrin is the inhibition of the classical complement pathway. This study reports that antimicrobial peptides derived from the N-terminal region from both human and bovine lactoferrin, lactoferricin H and lactoferricin B, respectively, inhibit the classical complement pathway. No inhibitory effect of these peptides was observed on the alternative complement pathway in an AP50 assay. However, lactoferricin B reduced the inhibitory properties of serum against *Escherichia coli* in a concentration dependent manner. These results suggest that the N-terminal region of lactoferrin is the important part in the inhibition of complement activation and that these peptides possess other important properties than their antimicrobial effect. Copyright 2004 Federation of European Microbiological Societies. Published by Elsevier B.V. All rights reserved.

L11 ANSWER 15 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:891963 CAPLUS  
DOCUMENT NUMBER: 139:374981  
TITLE: Antimicrobial peptides potentiate the activity of triazole antimicrobial agent, fluconazole  
INVENTOR(S): Nibbering, Petrus Hendricus; Lupetti, Antonella  
PATENT ASSIGNEE(S): AM-Pharma B. V., Neth.  
SOURCE: Eur. Pat. Appl., 23 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 1360961	A1	20031112	EP 2002-76804	20020507
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			EP 2002-76804	20020507
AB The invention describes a combination of at least two antimicrobial agents for the preparation of a medicament for the treatment of an infection of microbes in a subject in need thereof, the microbes being resistant to the first antimicrobial agent, the second antimicrobial agent comprising an antimicrobial peptide and a second antimicrobial agent, a medicament comprising an antimicrobial peptide for treating a microbial infection, and the use of a microbistatic agent and an antimicrobial peptide for the preparation of a microbicidic agent. The synergistic effect of above combination has been shown in the invention to treat infection of <i>Candida albicans</i> .				

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 16 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2003:404367 CAPLUS  
DOCUMENT NUMBER: 140:82103  
TITLE: Release of antimicrobial peptide Dhvar-5 from polymethyl methacrylate beads  
AUTHOR(S): Faber, C.; Stallmann, H. P.; Lyaruu, D. M.; de Blieck, J. M. A.; Bervoets, Th. J. M.; van Nieuw Amerongen, A.; Wuisman, P. I. J. M.  
CORPORATE SOURCE: Department of Orthopaedic Surgery, Vrije Universiteit Medical Center, Amsterdam, Neth.  
SOURCE: Journal of Antimicrobial Chemotherapy (2003), 51(6), 1359-1364  
CODEN: JACHDX; ISSN: 0305-7453

PUBLISHER: Oxford University Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Osteomyelitis is still a major cause of morbidity and remains a difficult complication to treat in orthopedic surgery. The treatment of choice is a combination of systemic and local antibiotics. The insertion of gentamicin-loaded polymethylmethacrylate (PMMA) beads into the bone results in high local concns. of gentamicin and low systemic concns. However, the effectiveness of this treatment is being hampered by the emergence of antimicrobial resistance. New antimicrobial agents are therefore needed. One new class of promising antibiotics is antimicrobial peptides (AMP). Derived from natural human peptides, these have a low tendency to induce antimicrobial resistance. Dhvar-5 is an antimicrobial peptide based on histatin-5, which is found in human saliva and consists of 14 amino acids. It has demonstrated bactericidal activity in vitro. In order to develop a new local treatment using Dhvar-5 for osteomyelitis, we investigated its release from PMMA beads and its antimicrobial activity against a clin. isolate of methicillin-resistant *Staphylococcus aureus* (MRSA) before and after release from PMMA beads. Specific amts. of Dhvar-5 were incorporated into PMMA mini beads, containing 120, 600 and 1200 µg of Dhvar-5, resp. Dhvar-5 was released from the beads in all three groups. Total release from the 120 µg beads was 9 µg per bead after 7 days. However, the release per bead in the 600 and 1200 µg beads was far more, resp., 416 and 1091 µg over a 28 day period. After release, the Dhvar-5 also retained its antimicrobial activity against MRSA. On the basis of these data we conclude that the amount of Dhvar-5 release from PMMA beads is not proportionate to the amount incorporated; instead, it demonstrated an exponential relationship to the amount of total peptide released. Furthermore, the released peptide remained biol. active against a clin. isolate of MRSA.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 17 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:883777 CAPLUS

DOCUMENT NUMBER: 141:42750

TITLE: Continuous-release or burst-release of the antimicrobial peptide human lactoferrin 1-11 (hLF1-11) from calcium phosphate bone substitutes

AUTHOR(S): Stallmann, Hein P.; Faber, Christopher; Slotema, Eveline T.; Lyaruu, D. M.; Bronckers, Antonius L. J. J.; Nieuw Amerongen, Arie V.; Wuisman, Paul I. J. M.

CORPORATE SOURCE: Department of Orthopaedic Surgery/VU University Medical Center, Amsterdam, 1007 MB, Neth.

SOURCE: Journal of Antimicrobial Chemotherapy (2003), 52(5), 853-855

CODEN: JACHDX; ISSN: 0305-7453

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In order to identify possible drug delivery systems against resistant bone infection, we determined the release of the antimicrobial peptide (AMP) human lactoferrin 1-11 (hLF1-11) from com. available bone substitutes. We combined six calcium phosphate cements and six granule-types with 5 mg/g hLF1-11 and measured its availability and release in vitro from cements (7 days) and granules (3 days). The integrity and antimicrobial activity of the hLF1-11 that was released during the first 24 h were measured, using mass spectrometry, and a killing assay on methicillin-resistant *Staphylococcus aureus* (MRSA). Most of the cements showed burst release followed by low-level continuous release, whereas the coated granules showed high burst release for 24 h. After release the peptide was active (in nine of 12 materials) and intact. Different release profiles may be obtained by choosing the appropriate carrier, which supports the feasibility of biodegradable carriers releasing AMPs against resistant infections.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 18 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2003:781138 CAPLUS  
DOCUMENT NUMBER: 140:300303  
TITLE: Degradation of antimicrobial histatin-variant peptides in Staphylococcus aureus and Streptococcus mutans  
AUTHOR(S): Groenink, J.; Ruissen, A. L. A.; Lowies, D.; Van't Hof, W.; Veerman, E. C. I.; Nieuw Amerongen, A. V.  
CORPORATE SOURCE: Department of Dental Basic Sciences, Section of Oral Biochemistry, Academic Centre for Dentistry Amsterdam (ACTA), Amsterdam, 1081 BT, Neth.  
SOURCE: Journal of Dental Research (2003), 82(9), 753-757  
CODEN: JDREAF; ISSN: 0022-0345  
PUBLISHER: International Association for Dental Research  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Histidine-free variants of salivary histatin 5 have a broad antimicrobial activity against various bacteria. In relation to a possible therapeutic application, we were interested in the susceptibility of these small peptides (14 amino acids long) to microbial proteinases and whether this affects their antimicrobial activity. Analyses by SDS-PAGE of supernatants of peptide-bacteria incubation showed a reduction in protein bands within 15 min incubation, as a result of cellular internalization. Degradation products of the variants dhvar1 and dhvar2 appeared within one hour in the supernatants of Streptococcus mutans and Staphylococcus aureus. In contrast, the variants dhvar3 and dhvar4 were more resistant to degradation under the same conditions. MALDITOF analyses identified cleavage of dhvar1 and dhvar2 at Glu6. The N-terminal peptide part (1-6) of dhvar1 and dhvar2 showed no bactericidal activity, while peptide fragment (7-14) showed a highly reduced bactericidal activity.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 19 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2003:969204 CAPLUS  
DOCUMENT NUMBER: 141:248584  
TITLE: The Influence of Antimicrobial Peptides and Mucolytics on the Integrity of Biofilms Consisting of Bacteria and Yeasts as Affecting Voice Prosthetic Air Flow Resistances  
AUTHOR(S): Oosterhof, Janine; Elving, G. Jolanda; Stokroos, Ietse; Van Nieuw Amerongen, Arie; Van Der Mei, Henny; Busscher, Henk; Van Weissenbruch, Ranny; Albers, Frans  
CORPORATE SOURCE: Department of Biomedical Engineering, University of Groningen, Groningen, 9713 AV, Neth.  
SOURCE: Biofouling (2003), 19(6), 347-353  
CODEN: BFOUEC; ISSN: 0892-7014  
PUBLISHER: Taylor & Francis Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The integrity of biofilms on voice prostheses used to rehabilitate speech in laryngectomized patients causes unwanted increases in airflow resistance, impeding speech. Biofilm integrity is ensured by extracellular polymeric substances (EPS). This study aimed to determine whether synthetic salivary peptides or mucolytics, including N-acetylcysteine and ascorbic acid, influence the integrity of voice prosthetic biofilms. Biofilms were grown on voice prostheses in an artificial throat model and exposed to synthetic salivary peptides, mucolytics and two different antiseptics (chlorhexidine and Triclosan). Synthetic salivary peptides did not reduce the air flow resistance of voice prostheses after biofilm formation. Although both chlorhexidine and Triclosan reduced microbial nos. on the prostheses, only the Triclosan-containing pos. control reduced the air flow resistance. Unlike

ascorbic acid, the mucolytic N-acetylcysteine removed most EPS from the biofilms and induced a decrease in air flow resistance.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 20 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:26947 CAPLUS

DOCUMENT NUMBER: 138:234670

TITLE: Synergistic activity of the N-terminal peptide of human lactoferrin and fluconazole against *Candida* species

AUTHOR(S): Lupetti, Antonella; Paulusma-Annema, Akke; Welling, Mick M.; Dogterom-Ballering, Heleen; Brouwer, Carlo P. J. M.; Senesi, Sonia; Van Dissel, Jaap T.; Nibbering, Peter H.

CORPORATE SOURCE: Department of Infectious Diseases, Leiden University Medical Center, Leiden, 2300 RC, Neth.

SOURCE: Antimicrobial Agents and Chemotherapy (2003), 47(1), 262-267

CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In light of the need for new antifungal regimens, we report that at noncandidacidal concns., the lactoferrin-derived peptide hLF(1-11), which is highly active against fluconazole-resistant *Candida albicans*, acts synergistically with fluconazole against this yeast and a fluconazole-sensitive *C. albicans* strain as well as *C. glabrata*, *C. krusei*, *C. parapsilosis*, and *C. tropicalis*. When these yeasts were exposed to hLF(1-11) for 5 min and then incubated with fluconazole, they were killed effectively, while no candidacidal activity was observed when they were incubated first with fluconazole and then exposed to the peptide, indicating that the candidacidal activity is initiated by the peptide while fluconazole is only required during the effector phase. Investigations of the effect of azide, which inhibits mitochondrial respiration, on the activity of combinations of hLF(1-11) and fluconazole against fluconazole-resistant *C. albicans* revealed that it inhibits this activity, even when added during the effector phase only. As expected, azide inhibited the accumulation of rhodamine 123 in mitochondria and the production and release of ATP by *C. albicans* that occurred upon exposure to the combination of hLF(1-11) and fluconazole. Accordingly, oxidized ATP (oATP), an antagonist of ATP receptors, completely blocked the candidacidal activity of the hLF(1-11)-fluconazole combination, whereas oATP did not block the activity when its presence was restricted to the effector phase. The candidacidal activity of combinations of hLF(1-11) and fluconazole, which is initiated by the peptide through the involvement of energized mitochondria, renders fluconazole-resistant *C. albicans* sensitive to this azole.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 21 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:310606 CAPLUS

DOCUMENT NUMBER: 139:304391

TITLE: Internalisation and degradation of histatin 5 by *Candida albicans*

AUTHOR(S): Ruissen, Anita L. A.; Groenink, Jasper; Krijtenberg, Patricia; Walgreen-Weterings, Els; van't Hof, Wim; Veerman, Enno C. I.; Nieuw Amerongen, Arie V

CORPORATE SOURCE: Department of Dental Basic Sciences, Section of Oral Biochemistry, Academic Centre for Dentistry Amsterdam (ACTA), Vrije Universiteit, Amsterdam, NL-1081 BT, Neth.

SOURCE: Biological Chemistry (2003), 384(1), 183-190  
CODEN: BICHF3; ISSN: 1431-6730

PUBLISHER: Walter de Gruyter GmbH & Co. KG  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Histatins, salivary antimicrobial peptides, are susceptible to proteolytic degradation, often ascribed to host proteinases. In this study, we addressed the question whether proteolytic activity from microbial sources can contribute to this degradation. *Candida albicans*, an opportunistic yeast that is susceptible to the histatins, was used as target organism. The most potent histatin (histatin 5: sequence: DSHAKRHHGYKRKFHEKHHSHRGY), two histatin 5 fragments (dh-5: sequence: KRKFHEKHHSHRGY; P-113: sequence: AKRHHGYKRKFH) and an all-D isomer of the latter (P-113D) were used as model peptides. All L-peptides were susceptible to degradation by *C. albicans*. Cleavage was established at Lys5 and His19 of histatin 5, Lys11, Arg12, Phe14, Glu16, Lys17, His18 and Ser20 of dh-5 and Ala4 and Lys11 of P-113. In addition, it was found that secreted *C. albicans* enzymes are not involved in the degradation process and that blocking cell entry of the peptides greatly impedes degradation. Moreover, P-113D, which is biol. as active as P-113, was hardly susceptible to proteolysis. These data imply that proteolysis occurs mainly intracellularly and is not used as a protective mechanism against histatin activity. Together, our results suggest that, besides host proteinases, microbial enzymes play an important role in histatin degradation.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 22 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:591671 CAPLUS

DOCUMENT NUMBER: 137:145637

TITLE: Novel bone cement containing bone growth factor and antimicrobial agent

INVENTOR(S): Burger, Elisabeth Henriette

PATENT ASSIGNEE(S): Am-Pharma B.V., Neth.

SOURCE: Eur. Pat. Appl., 17 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1228772	A1	20020807	EP 2001-200363	20010201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CA 2436420	AA	20020808	CA 2002-2436420	20020129
WO 2002060503	A1	20020808	WO 2002-EP947	20020129
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1359946	A1	20031112	EP 2002-710818	20020129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517700	T2	20040617	JP 2002-560694	20020129
US 2004131678	A1	20040708	US 2003-627314	20030725
PRIORITY APPLN. INFO.:			EP 2001-200363	A 20010201
			WO 2002-EP947	W 20020129

AB A water-based bone substitute for in vivo implantation, promoting bone tissue growth in situ comprises bone substitute material, a slow release

bone growth factor and a fast release antimicrobial agent. Further, a kit and a method for the preparation of the bone substitute is disclosed. For example, 1 mg antimicrobial peptide DHVAR-5 (LLLFLKKRKKRKY, Seq ID No 4) was mixed with 1 g Biobon cement powder. The transforming growth factor- $\beta$  (TGF $\beta$ ) was suspended in a solution of 0.2% serum albumin in 4 mM HCl, at 1  $\mu$ g TGF $\beta$ /mL solution, forming the first aqueous medium. This suspension was mixed with an equal volume of a second aqueous medium, comprising 4% Na<sub>2</sub>HPO<sub>4</sub>. Both first and second media were combined and mixed. One gram of the dry component, DHVAR-5 enriched cement powder, was mixed with 0.8 mL of the liquid component, TGF $\beta$  enriched cement liquid to give a moldable paste that hardens within 5 min. The bone substitute obtained comprised 1 mg antimicrobial peptide and 0.4  $\mu$ g TGF $\beta$  per 1 g cement.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 23 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:69326 CAPLUS

DOCUMENT NUMBER: 136:97828

TITLE: Antimicrobial peptides for food, hygienic products, disinfectants, cleaning agents and biocides

INVENTOR(S): Keijser, Ewald Clemens Raphael Maria

PATENT ASSIGNEE(S): Hom Consultancy B.V., Neth.

SOURCE: Eur. Pat. Appl., 11 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1174027	A1	20020123	EP 2000-202562	20000717
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: EP 2000-202562 20000717

AB Described are novel uses of antimicrobial peptides or proteins, comprising an amino acid domain, chosen from the group, consisting of the following amino acid sequences: KRLFKKLKFSRLRKY, KRLFKLLFSLRKY, LLLFLKKRKKRKY, or an amino acid domain sharing at least 40% identity therewith, as active ingredient in an antimicrobial preparation for surface treatment of articles to counteract microbial growth on the said surface, and as additive in human and animal food, hygienic care products, disinfectants, cleaning agents and biocides. Further a transgenic plant expressing the amino acid sequence is disclosed.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 24 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:414493 CAPLUS

DOCUMENT NUMBER: 137:137430

TITLE: Internal thiols and reactive oxygen species in candidacidal activity exerted by an N-terminal peptide of human lactoferrin

AUTHOR(S): Lupetti, Antonella; Paulusma-Annema, Akke; Senesi, Sonia; Campa, Mario; Van Dissel, Jaap T.; Nibbering, Peter H.

CORPORATE SOURCE: Department of Infectious Diseases, Leiden University Medical Center, Leiden, 2300 RC, Neth.

SOURCE: Antimicrobial Agents and Chemotherapy (2002), 46(6), 1634-1639

CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We previously showed that the energized mitochondrion and extracellular ATP are essential for the candidacidal activity of the N-terminal peptide of human lactoferrin, subsequently referred to as hLF(1-11). The present study focuses on the involvement of internal thiols and reactive O spp. (ROS) in the candidacidal activity exerted by hLF(1-11). hLF(1-11) Reduced the internal thiol level of *Candida albicans* by 20%. In agreement, N-acetyl-L-cysteine (NAC), which is a precursor of glutathione and an ROS scavenger, inhibited the candidacidal activity of hLF(1-11). In addition, azodicarboxylic acid bis(N,N-dimethylamide) (diamide), which oxidizes internal thiols, was candidacidal. Furthermore, hLF(1-11) increased the level of ROS production by *C. albicans* in a dose-dependent manner, and a correlation between ROS production and candidacidal activity was found. 6-Hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (trolox), which is an ROS scavenger, partially inhibited the hLF(1-11)-induced, but not the diamide-triggered, candidacidal activity. It is of interest that hLF(1-11) and diamide acted synergistically in killing *C. albicans* and in ROS production. In agreement, oxidized ATP, an irreversible inhibitor of extracellular ATP receptors, partially blocked the hLF(1-11)-induced, but not the diamide-triggered, candidacidal activity. Finally, the hLF(1-11)-induced activation of mitochondria was inhibited by NAC, indicating that internal thiols and ROS affect mitochondrial activity. Therefore, the candidacidal activity of hLF(1-11) involves both generation of ROS and reduction of internal thiols.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 25 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2002:636010 CAPLUS

DOCUMENT NUMBER: 137:261541

TITLE: Histatin 5 and derivatives. Their localization and effects on the ultra-structural level

AUTHOR(S): Ruissen, A. L. A.; Groenink, J.; Van 't Hof, W.; Walgreen-Weterings, E.; van Marle, J.; van Veen, H. A.; Voorhout, W. F.; Veerman, E. C. I.; Nieuw Amerongen, A. V.

CORPORATE SOURCE: Academic Centre for Dentistry Amsterdam, Department of Dental Basic Sciences, Vrije Universiteit, Amsterdam, 1081 BT, Neth.

SOURCE: Peptides (New York, NY, United States) (2002), 23(8), 1391-1399

CODEN: PPTDD5; ISSN: 0196-9781

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Histatins, a family of cationic peptides present in saliva, are active against the opportunistic yeast *Candida albicans*. The mechanism of action is still unclear. Histatin 5 and more potent synthetic variants, dhvar4 and dhvar5, were used to study localization and effects on morphol. on the ultra-structural level. Although all peptides induced leakage, no association with the plasma membrane, indicative for permanent pores, was observed with immuno-gold-labeling. Freeze-fracturing showed severe changes of the plasma membrane. Together with, for the dhvars, the loss of intracellular integrity, this suggests that leakage may be a secondary effect rather than an effect of formation of permanent pores.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 26 OF 63 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:443047 BIOSIS

DOCUMENT NUMBER: PREV200200443047

TITLE: Structure function analysis of lactoferricin variants.

AUTHOR(S): Chapple, D. D. [Reprint author]; Hussain, R.; Moriarty, L.; Joannou, C.; Odell, E.; Siligardi, G.; Evans, R. W.

CORPORATE SOURCE: King's College London, London, UK

SOURCE: Biochemistry and Cell Biology, (2002) Vol. 80, No. 1, pp. 166. print.  
Meeting Info.: 5th International Conference on Lactoferrin: Structure, Function and Applications. Banff, Alberta, Canada. May 04-09, 2001.  
CODEN: BCBIEQ. ISSN: 0829-8211.

DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 21 Aug 2002  
Last Updated on STN: 23 Sep 2002

L11 ANSWER 27 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:581749 CAPLUS

DOCUMENT NUMBER: 135:157726

TITLE: Medical device coated with antimicrobial peptides

INVENTOR(S): Van Nieuw, Amerongen Arie; Veerman, Engelmundus Cornelis Ignatius; Van't Hof, Willem

PATENT ASSIGNEE(S): Am-Pharma B.V., Neth.

SOURCE: PCT Int. Appl., 22 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001056627	A1	20010809	WO 2001-NL19	20010112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: NL 2000-1008734 A 20000112

AB Described is a medical device for application onto or into a body of a patient, coated with one or more naturally occurring peptides or proteins or synthetic peptides and analogs thereof having antimicrobial activity. The antimicrobial peptides and proteins are preferably chosen from the group, consisting of cystatin-derived peptides, histatin-derived peptides, lactoferrin-derived peptides and specific proteinase inhibitors.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 28 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:360032 CAPLUS

DOCUMENT NUMBER: 134:371750

TITLE: Antimicrobial activity of the first cationic cluster of human lactoferrin

INVENTOR(S): Van Berkel, Patrick Hendrikus Cornelis; Nibbering, Peter Hendrikus; Nuijens, Jan Henricus

PATENT ASSIGNEE(S): Pharming Intellectual Property B.V., Neth.

SOURCE: PCT Int. Appl., 59 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001034641	A2	20010517	WO 2000-NL821	20001110
WO 2001034641	A3	20020214		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2388910	AA	20010517	CA 2000-2388910	20001110
EP 1228097	A2	20020807	EP 2000-981916	20001110
EP 1228097	B1	20051221		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2003521483	T2	20030715	JP 2001-537352	20001110
AU 776044	B2	20040826	AU 2001-19015	20001110
AT 313562	E	20060115	AT 2000-981916	20001110
PT 1228097	T	20060531	PT 2000-981916	20001110
ES 2256070	T3	20060716	ES 2000-981916	20001110
US 7060677	B1	20060613	US 2002-130180	20020510

PRIORITY APPLN. INFO.:

EP 1999-203775	A	19991111
US 1999-164975P	P	19991111
WO 2000-NL821	W	20001110

AB The present invention provides polypeptides related to human lactoferrin protein that have utility in a variety of therapeutic and prophylactic applications, including use as antimicrobial agents. The invention further provides pharmaceutical compns. containing these polypeptides and therapeutic methods using such compns. Methods for detecting antimicrobial infections using the polypeptides are also provided.

L11 ANSWER 29 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:215858 CAPLUS

DOCUMENT NUMBER: 134:292646

TITLE: Human lactoferrin and peptides derived from its N terminus are highly effective against infections with antibiotic-resistant bacteria

AUTHOR(S): Nibbering, P. H.; Ravensbergen, E.; Welling, M. M.; Van Berkel, L. A.; Van Berkel, P. H. C.; Pauwels, E. K. J.; Nuijens, J. H.

CORPORATE SOURCE: Department of Infectious Diseases, Leiden University Medical Center, Leiden, 2300 RC, Neth.

SOURCE: Infection and Immunity (2001), 69(3), 1469-1476  
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Since human lactoferrin (hLF) binds to bacterial products through its highly pos. charged N terminus, we investigated which of the two cationic domains is involved in its bactericidal activity. The results revealed that hLF lacking the first three residues (hLF-3N) was less efficient than hLF in killing of antibiotic-resistant *Staphylococcus aureus*, *Listeria monocytogenes*, and *Klebsiella pneumoniae*. Both hLF preps. failed to kill *Escherichia coli* O54. In addition, hLF-3N was less effective than hLF in reducing the number of viable bacteria in mice infected with antibiotic-resistant *S. aureus* and *K. pneumoniae*. Studies with synthetic peptides corresponding to the first 11 N-terminal amino acids, designated hLF(1-11), and fragments thereof demonstrated that peptides lacking the first three N-terminal residues are less effective than hLF(1-11) in killing of bacteria. Furthermore, a peptide corresponding to residues 21 to 31, which comprises the second cationic domain, was less effective than hLF(1-11) in killing of bacteria in vitro and in mice having an infection with antibiotic-resistant *S. aureus* or *K. pneumoniae*. Using fluorescent probes, we found that bactericidal hLF peptides, but not nonbactericidal

peptides, caused an increase of the membrane permeability. In addition, hLF killed the various bacteria, most probably by inducing intracellular changes in these bacteria without affecting the membrane permeability. Together, hLF and peptides derived from its N terminus are highly effective against infections with antibiotic-resistant *S. aureus* and *K. pneumoniae*, and the first two arginines play an essential role in this activity.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 30 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:702152 CAPLUS

DOCUMENT NUMBER: 136:275454

TITLE: 99mTc-labeled antimicrobial peptides for detection of bacterial and *Candida albicans* infections

AUTHOR(S): Welling, Mick M.; Lupetti, Antonella; Balter, Henia S.; Lanzzeri, Stella; Souto, Beatriz; Rey, Ana M.; Savio, Eduardo O.; Paulusma-Annema, Akke; Pauwels, Ernest K. J.; Nibbering, Peter H.

CORPORATE SOURCE: Departments of Radiology and Infectious Diseases, Leiden University Medical Center, Leiden, Neth.

SOURCE: Journal of Nuclear Medicine (2001), 42(5), 788-794  
CODEN: JNMEAQ; ISSN: 0161-5505

PUBLISHER: Society of Nuclear Medicine

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This study compared the possibilities and limitations of 99mTc-labeled synthetic peptides derived from two human antimicrobial peptides, namely, ubiquicidin (UBI) and lactoferrin (hLF), for the scintigraphic detection of bacterial and fungal infections in mice and rabbits. The rationale of our approach was that selected peptides accumulate in infected areas but not in sterile inflammatory lesions, because they bind preferentially to microorganisms. 99mTc-labeled human neutrophil peptides (defensins), ciprofloxacin, and human polyclonal IgG were included as control agents. Methods: 99mTc-labeled peptides and control agents were injected i.v. into animals that had been injected i.m. 18 h earlier with multidrug-resistant *Staphylococcus aureus*, *Klebsiella pneumoniae*, or fluconazole-resistant *Candida albicans*. Sterile inflammatory sites were induced by the injection of heat-killed microorganisms or lipo-polysaccharide (LPS) into the thigh muscle. Up to 4 h after injection, the accumulation of 99mTc-labeled compds. in the infected/inflamed thigh muscles was determined using scintigraphic techniques and radioactivity counts in dissected tissues. Results: Scintigraphy revealed that 99mTc-labeled peptides UBI 29-41, UBI 18-35, UBI 31-38, hLF 1-11, and defensins, which showed preferential in vitro binding to microorganisms in a former study, accumulated at a significantly higher rate ( $P < 0.01$ ) in bacterial and *C. albicans* infections in mice and rabbits than in inflamed tissues induced by heat-killed microorganisms or by LPS. No significant difference in the accumulation of 99mTc-labeled ciprofloxacin was observed between infected and sterile inflamed thigh muscles in mice. Conclusion: 99mTc-labeled antimicrobial peptides UBI 29-41, UBI 18-35, UBI 31-38, hLF 1-11, and defensins accumulate significantly in tissues infected with gram-pos. and gram-neg. bacteria and *C. albicans*. Significantly lower ( $P < 0.01$ ) accumulation of these peptides occurs in sterile inflamed tissues. These data indicate that the peptides preferentially tag microorganisms at the site of infection, which is in agreement with their preferential binding to the microorganisms in vitro and in vivo. 99mTc-labeled ciprofloxacin does not distinguish between infections and sterile inflammatory lesions, which implies that its specificity for the detection of bacterial infections is not warranted.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 31 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2001:462667 CAPLUS

DOCUMENT NUMBER: 135:192715  
TITLE: Effects of histatin 5 and derived peptides on *Candida albicans*  
AUTHOR(S): Ruissen, Anita L. A.; Groenink, Jasper; Helmerhorst, Eva J.; Walgreen-Weterings, Els; Van't Hof, Wim; Veerman, Enno C. I.; Nieuw Amerongen, Arie V.  
CORPORATE SOURCE: Department of Dental Basic Sciences, Section of Oral Biochemistry, Academic Centre for Dentistry Amsterdam (ACTA), Amsterdam, 1081 BT, Neth.  
SOURCE: Biochemical Journal (2001), 356(2), 361-368  
CODEN: BIJOAK; ISSN: 0264-6021  
PUBLISHER: Portland Press Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Three anti-microbial peptides were compared with respect to their killing activity against *Candida albicans* and their ability to disturb its cellular and internal membranes. Histatin 5 is an anti-fungal peptide occurring naturally in human saliva, while dhvar4 and dhvar5 are variants of its active domain, with increased anti-microbial activity. Dhvar4 has increased amphipathicity compared with histatin 5, whereas dhvar5 has amphipathicity comparable with that of histatin 5. All three peptides caused depolarization of the cytoplasmic and/or mitochondrial membrane, indicating membranolytic activity. For the variant peptides both depolarization and killing occurred at a faster rate. With FITC-labeled peptides, no association with the cytoplasmic membrane was observed, contradicting the formation of permanent transmembrane multimeric peptide pores. Instead, the peptides were internalized and act on internal membranes, as demonstrated with mitochondrion- and vacuole-specific markers. In comparison with histatin 5, the variant peptides showed a more destructive effect on mitochondria. Entry of the peptides and subsequent killing were dependent on the metabolic state of the cells. Blocking of the mitochondrial activity led to complete protection against histatin 5 activity, whereas that of dhvar4 was hardly affected and that of dhvar5 was affected only intermediately.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 32 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:819423 CAPLUS  
DOCUMENT NUMBER: 138:235228  
TITLE: Expression of human lactoferricin in HC11 cells  
AUTHOR(S): Nam, Myoung-Soo  
CORPORATE SOURCE: Div. Animal Sci. Resources, College Agriculture Life Sci., Chungnam National Univ., Daejeon, 305-764, S. Korea  
SOURCE: Nongop Kwahak Yongu (Chungnam Taehakkyo) (2001), 28(2), 92-98  
CODEN: NKYOE7; ISSN: 1225-2220  
PUBLISHER: Chungnam National University, College of Agriculture  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Lactoferricin is an antibacterial peptide fragment (about 5 kD) derived from lactoferrin (80 kD) that displays the various biol. functions. The production of a human lactoferricin (Lactoferricin H) in mouse HC11 mammary epithelial cells was achieved by placing its cDNA under the control of the bovine  $\beta$ -casein gene. To express lactoferricin H in this cell culture system, constructed a hybrid-splice signal consisting of bovine  $\beta$ -casein intron I and rabbit  $\beta$ -globin intron II, and a DNA fragment spanning intron 8 of the bovine  $\beta$ -casein gene. Expression of lactoferricin H from this expression vector was identified by RT-PCR, northern and dot blot anal. RT-PCR using total RNA of HC11 cells transfected with pBL1-cin expression vector yielded a product identified as having a size of the 150 bp. Northern blot anal. was identified about 2.3 kb. In dot blot anal., recombinant lactoferricin H was recognized with anti-human lactoferrin polyclonal antibody.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 33 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2000:384233 CAPLUS  
DOCUMENT NUMBER: 133:26840  
TITLE: Antiviral peptides for treatment of viral infections  
INVENTOR(S): Van Nieuw Amerongen, Arie; Veerman, Engelmundus  
Cornelis Ignatius; Van't Hof, Willem; Nibbering, Peter  
Hendricus  
PATENT ASSIGNEE(S): Stichting voor de Technische Wetenschappen, Neth.  
SOURCE: PCT Int. Appl., 20 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032629	A2	20000608	WO 1999-NL732	19991201
WO 2000032629	A3	20000817		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
NL 1010692	C2	20000606	NL 1998-1010692	19981201
CA 2353530	AA	20000608	CA 1999-2353530	19991201
EP 1147132	A2	20011024	EP 1999-960013	19991201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002531465	T2	20020924	JP 2000-585269	19991201
US 2002111305	A1	20020815	US 2001-872864	20010601
PRIORITY APPLN. INFO.: NL 1998-1010692 A 19981201				
WO 1999-NL732 W 19991201				
AB The invention relates to peptides for use as antiviral agent, consisting of an amino acid chain which contains a domain of 10 to 25 amino acids, wherein the majority of the amino acids of the one half of the domain are pos. charged amino acids and the majority of the amino acids of the other half of the domain are uncharged amino acids. The invention further relates to oligomers of these peptides consisting of at least two such peptides which are coupled to each other, optionally via a spacer, for use as antiviral agent, in addition to the use of the peptides and/or oligomers for the manufacture of a medicine for treating viral infections.				

L11 ANSWER 34 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2000:34776 CAPLUS  
DOCUMENT NUMBER: 132:113127  
TITLE: Bone cement with antimicrobial peptides  
INVENTOR(S): Burger, Elisabeth Henriette; Van Nieuw Amerongen, Arie; Wuisman, Paulus Ignatius Jozef Maria  
PATENT ASSIGNEE(S): Stichting Skeletal Tissue Engineering Group Amsterdam, Neth.  
SOURCE: PCT Int. Appl., 20 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2000001427	A1	20000113	WO 1999-NL417	19990702
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2336030	AA	20000113	CA 1999-2336030	19990702
AU 9948040	A1	20000124	AU 1999-48040	19990702
AU 762262	B2	20030619		
EP 1091774	A1	20010418	EP 1999-931589	19990702
EP 1091774	B1	20021030		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002519155	T2	20020702	JP 2000-557873	19990702
AT 226836	E	20021115	AT 1999-931589	19990702
PT 1091774	T	20030331	PT 1999-931589	19990702
ES 2186377	T3	20030501	ES 1999-931589	19990702
PRIORITY APPLN. INFO.:			EP 1998-202233	A 19980702
			WO 1999-NL417	W 19990702

AB The invention relates to bone material for the prevention and treatment of osteomyelitis, which material is provided with antimicrobial peptides (AMPs) consisting of an amino acid chain which contains a domain of 10 to 25 amino acids, wherein the majority of the amino acids of the one half of the domain are pos. charged amino acids and the majority of the amino acids of the other half of the domain are uncharged amino acids, which AMPs can be released to the surrounding area for a period of time and wherein the bone material forms bone cement after curing and the AMPs are distributed homogeneously in the cured bone cement. The invention further relates to a method of manufacturing the bone material, wherein the bone material is cured to bone cement and wherein the AMPs are distributed homogeneously in the cured bone cement.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 35 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:166140 CAPLUS

DOCUMENT NUMBER: 134:323332

TITLE: Candidacidal activities of human lactoferrin peptides derived from the N terminus

AUTHOR(S): Lupetti, Antonella; Paulusma-Annema, Akke; Welling, Mick M.; Senesi, Sonia; Van Dissel, Jaap T.; Nibbering, Peter H.

CORPORATE SOURCE: Department of Infectious Diseases, Leiden University Medical Center, Leiden, 2300 RC, Neth.

SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(12), 3257-3263

CODEN: AMACQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In light of the need for new antifungal agents, the candidacidal activities of human lactoferrin (hLF) and synthetic peptides representing the first, hLF(1-11), and second, hLF(21-31), cationic domains of its N terminus were compared. The results revealed that hLF(1-11) was more effective in killing fluconazole-resistant *Candida albicans* than hLF(21-31) and much more effective than lactoferrin, as determined microbiol. and by propidium iodide (PI) staining. By using hLF(1-11) and various derivs., it was found that the second and third residues of the N terminus of hLF(1-11) were critical for its candidacidal activity. Detailed investigation to elucidate the mechanism of action of hLF(1-11) revealed a

dose-dependent release of ATP by *Candida* upon exposure to hLF(1-11). Our observations that sodium azide reduced the PI uptake and candidacidal activity of hLF(1-11) and that, upon exposure to hLF(1-11), the fluorescent dye rhodamine 123 first accumulated inside the mitochondria and later was released into the cytoplasm indicate that the peptide triggers the energized mitochondrion. Furthermore, oxidized ATP, which interferes with the interaction of ATP with its extracellular receptors, blocked the candidacidal action of hLF(1-11), as measured microbiol. and by PI staining. Addition of ATP (or analogs) was not a sufficient stimulus to kill *C. albicans* or to act synergistically with suboptimal concns. of the peptide. The main conclusions are that the first two arginines at the N terminus of hLF are critical in the candidacidal activity of hLF(1-11) and that extracellular ATP is essential but not sufficient for the peptide to exert its candidacidal activity.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 36 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:138714 CAPLUS

DOCUMENT NUMBER: 132:345333

TITLE: Antimicrobial activity of synthetic salivary peptides against voice prosthetic microorganisms

AUTHOR(S): Elving, G. Jolanda; Van Der Mei, Henny C.; Busscher, Henk J.; Van Nieuw Amerongen, Arie; Veerman, Enno C. I.; Van Weissenbruch, Ranny; Albers, Frans W. J.

CORPORATE SOURCE: Departments of Biomedical Engineering and Otorhinolaryngology, University Hospital of Groningen, Groningen, Neth.

SOURCE: Laryngoscope (2000), 110(2, Pt. 1), 321-324

CODEN: LARYA8; ISSN: 0023-852X

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To investigate whether synthetic salivary antimicrobial peptides have an inhibitory effect on the growth of bacteria and yeasts isolated from used silicone rubber voice prostheses. The antimicrobial activities of six synthetic salivary peptides (histatin 5, dhvar1, dhvar4, dhvar5, lactoferrin b 17-30 [LFb 17-30], and cystatin S1-15) at concns. of 2 and 4 mg/mL were determined against different oropharyngeal yeast (four) and bacterial (eight) strains and against a "total microflora" isolated from explanted voice prostheses using agar diffusion tests. The spectrum of susceptible microorganisms was determined qual. Histatin 5 and cystatin S1-15 did not show any antimicrobial activity against the microorganisms involved in this study. Dhvar1 was active against some of the oropharyngeal microorganisms tested, including the yeast strains, but not against *Rothia dentocariosa*, *Staphylococcus aureus*, *Escherichia coli*, and the total microflora. Dhvar4 was active against all microorganisms tested, including the total microflora. Dhvar5 lacked activity against *E. coli* and the total microflora. LFb 17-30 did not inhibit the growth of any of the yeast strains involved and showed only minor activity against some of the bacterial strains. LFb 17-30 slightly inhibited the growth of the total microflora from an explanted prosthesis. The synthetic salivary peptide dhvar4 has a broad antimicrobial activity against all microorganisms that are commonly isolated from explanted voice prostheses, including yeasts. Therewith, it may represent a useful drug, as an alternative for antibiotics and antimycotics employed in various ways to prolong the lifetime of voice prostheses in laryngectomees.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 37 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:141414 CAPLUS

DOCUMENT NUMBER: 133:204794

TITLE: Technetium-99m labelled antimicrobial peptides discriminate between bacterial infections and sterile

inflammations  
AUTHOR(S): Welling, Mick M.; Paulusma-Annema, Akke; Balter, Henia S.; Pauwels, Ernest K. J.; Nibbering, Peter H.  
CORPORATE SOURCE: Division of Nuclear Medicine, Department of Radiology, Leiden University Medical Center (LUMC), Leiden, 2300 RC, Neth.  
SOURCE: European Journal of Nuclear Medicine (2000), 27(3), 292-301  
CODEN: EJNMD9; ISSN: 0340-6997  
PUBLISHER: Springer-Verlag  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The aim of this study was to select technetium-99m labeled peptides that can discriminate between bacterial infections and sterile inflammations. For this purpose, we first assessed the binding of various 99mTc-labeled natural or synthetic peptides, which are based on the sequence of the human antimicrobial peptide ubiquicidin (UBI) or human lactoferrin (hLF), to bacteria and to leukocytes in vitro. In order to select peptides that preferentially bind to bacteria over host cells, radiolabeled peptides were injected into mice i.p. infected with *Klebsiella pneumoniae* (*K. pneumoniae*) and the amount of radioactivity associated with the bacteria and with the leukocytes was quantitated. The next phase focussed on discrimination between bacterial infections and sterile inflammatory processes using 99mTc-labeled peptides in mice i.m. infected with various bacteria (e.g. multi-drug-resistant *Staphylococcus aureus*) and in animals that had been injected with lipopolysaccharides (LPS) of bacterial origin to create a sterile inflammatory process. Also, we studied the distribution of 99mTc-labeled UBI 29-41 and UBI 18-35 in rabbits having an exptl. thigh muscle infection with *K. pneumoniae* and in rabbits injected with LPS. Based on the results of our in vitro and in vivo binding assays, two peptides, i.e. UBI 29-41 and UBI 18-35, were selected as possible candidates for infection imaging. The radiolabeled peptides can detect infections with both gram-pos. and gram-neg. bacteria in mice as early as 5-30 min after injection, with a target-to-non-target (T/NT) ratio between 2 and 3; maximum T/NT ratios were seen within 1 h after injection. In rabbits, high T/NT ratios (>5) for 99mTc-labeled UBI 29-41 were observed from 1 h after injection. No accumulation of the selected 99mTc-labeled UBI-derived peptides was observed in thighs of mice and rabbits previously injected with LPS. Scintigraphic investigation into the biodistribution of 99mTc-labeled UBI peptides revealed that these peptides were rapidly removed from the circulation by renal excretion. Similar data were observed for 99mTc-labeled defensin 1-3. Our data for 99mTc-labeled hLF and related peptides indicate that these compds. are less favorable for infection detection. Taken together, 99mTc-labeled UBI 18-35 and UBI 29-41 enable discrimination between bacterial infections and sterile inflammatory processes in both mice and rabbits. Based on their characteristics, we consider these peptides the candidates of preference for detection of bacterial infections in man.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 38 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:98289 CAPLUS  
DOCUMENT NUMBER: 134:338097  
TITLE: Synergistic effects of low doses of histatin 5 and its analogues on amphotericin B anti-mycotic activity  
AUTHOR(S): Van't Hof, Wim; Reijnders, Ingrid M.; Helmerhorst, Eva J.; Walgreen-Weterings, Els; Simoons-Smit, Ina M.; Veerman, Enno C. I.; Nieuw Amerongen, Arie V.  
CORPORATE SOURCE: Academic Centre for Dentistry, Vrije Universiteit, Amsterdam, Neth.  
SOURCE: Antonie van Leeuwenhoek (2000), 78(2), 163-169  
CODEN: ALJMAO; ISSN: 0003-6072  
PUBLISHER: Kluwer Academic Publishers  
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The increase in the use of antifungal agents for prophylaxis and therapy has led to the development of antifungal drug resistance. Drug combinations may prevent or delay resistance development. The aim of the present study was to investigate whether naturally and designed cationic antifungal peptides act synergistically with commonly used antimycotics. No enhanced activity was found upon addition of dhvar4, a designed analog of the human salivary peptide histatin 5, or PGLa to fluconazole or 5-flucytosine, resp. In contrast, strong synergism of amphotericin B with the peptides was found against several *Aspergillus*, *Candida*, and *Cryptococcus* strains, and against an amphotericin B-resistant *C. albicans* laboratory mutant in the standardized broth microdilution assays according to the NCCLS standard method M27-T. Amphotericin B showed synergism with dhvar5, another designed analog of histatin 5, and with magainin 2 against all 7 tested strains. Combinations of amphotericin B with histatin 5, dhvar4, and PGLa showed synergism against 4 of the 7 strains. The growth inhibitory activity of amphotericin B was enhanced by sub-MIC concns. of peptide, but its hemolytic activity remained unaffected, suggesting that its cytotoxicity to host cells was not increased and that peptides may be suitable candidates for combination therapy.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 39 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:382948 CAPLUS

DOCUMENT NUMBER: 133:331151

TITLE: Approach to identification and comparison of the heparin-interacting sites of lactoferrin using synthetic peptides

AUTHOR(S): Shimazaki, K.; Uji, K.; Tazume, T.; Kumura, H.; Shimo-Oka, T.

CORPORATE SOURCE: Dairy Science Laboratory, Faculty of Agriculture, Hokkaido University, Sapporo, 060-8589, Japan

SOURCE: International Congress Series (2000), 1195(Lactoferrin: Structure, Function and Applications), 37-46  
CODEN: EXMDA4; ISSN: 0531-5131

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The affinity of lactoferrin for heparin is one its well-known properties. Certain consensus sequences have been proposed for other heparin-binding proteins, such as BBXB, BBBXB or BXXBBXB, where B denotes a pos. charged amino acid residue. The purpose of the present study was to identify the essential amino acid side chain groups of the lactoferrin mol. contributing to the interaction with heparin. The heparin-interacting properties of transferrin family proteins were compared by examining the heparin-binding activity of various peptides prepared by chemical synthesis. Each peptide was composed of 10-15 amino acid residues and was synthesized from Fmoc amino acid active esters on a pre-activated cellulose membrane using the SPOTs system. Each of the peptides was incubated with heparin. To detect heparin-interaction, human vitronectin and alkaline phosphatase-conjugated anti-vitronectin monoclonal antibody were used. Peptides corresponding to partial sequences of human, bovine, pig and goat lactoferrins, human transferrin, chicken ovotransferrin and human melanotransferrin were studied. The results obtained were as follows: of the two BXB sequences in the bovine lactoferrin N-lobe, KCRR (18-21) and RMKK (25-28), the latter was found to be essential for interaction with heparin; the BXB sequence in the C-lobe did not interact with heparin; BXB and BBXB sequences in human transferrin showed no interaction with heparin. These results were consistent with findings obtained in affinity chromatog. expts. using an immobilized heparin column.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



L11 ANSWER 40 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:487322 CAPLUS  
DOCUMENT NUMBER: 131:127561  
TITLE: Antimicrobial peptides  
INVENTOR(S): Van Nieuw Amerongen, Arie; Veerman, Engelmundus  
Cornelis Ignatius; Van't Hof, Willem; Helmerhorst, Eva  
Josephine  
PATENT ASSIGNEE(S): Stichting Voor De Technische Wetenschappen, Neth.  
SOURCE: PCT Int. Appl., 29 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9937678	A2	19990729	WO 1999-NL45	19990126
WO 9937678	A3	19991014		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
NL 1008139	C2	19990728	NL 1998-1008139	19980127
CA 2319094	AA	19990729	CA 1999-2319094	19990126
AU 9923014	A1	19990809	AU 1999-23014	19990126
AU 759026	B2	20030403		
EP 1051433	A2	20001115	EP 1999-902926	19990126
EP 1051433	B1	20041006		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
JP 2003524578	T2	20030819	JP 2000-528598	19990126
AT 278710	E	20041015	AT 1999-902926	19990126
ES 2229669	T3	20050416	ES 1999-902926	19990126
US 6638531	B1	20031028	US 2000-601124	20001013
PRIORITY APPLN. INFO.:			NL 1998-1008139	A 19980127
			WO 1999-NL45	W 19990126
AB	The invention relates to peptides with antimicrobial activity, consisting of an amino acid chain which contains a domain of 10-25 amino acids, wherein the majority of the amino acids of the one half of the domain are pos. charged amino acids and the majority of the amino acids of the other half of the domain are uncharged amino acids.			

L11 ANSWER 41 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:224531 CAPLUS  
DOCUMENT NUMBER: 130:316617  
TITLE: Antimicrobial agents containing new quinolone-type bactericides and lactoferrin peptides  
INVENTOR(S): Kamata, Shinichi  
PATENT ASSIGNEE(S): Morinaga Milk Industry Co., Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp..  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11092375	A2	19990406	JP 1997-278113	19970925

PRIORITY APPLN. INFO.: JP 1997-278113 19970925  
AB Antimicrobial agents showing enhanced effects contain new quinolone-type bactericides and lactoferrin peptides. An injection was formulated containing lomefloxacin 0.001, lactoferrin peptide 0.05 and sodium chloride 10 mg with addition of injection water to 1 mL.

L11 ANSWER 42 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:775763 CAPLUS  
DOCUMENT NUMBER: 132:146210  
TITLE: Permeabilizing action of an antimicrobial lactoferricin-derived peptide on bacterial and artificial membranes  
AUTHOR(S): Aguilera, O.; Ostolaza, H.; Quiros, L. M.; Fierro, J. F.  
CORPORATE SOURCE: Laboratory of Oral Microbiology, School of Stomatology, Oviedo, Spain  
SOURCE: FEBS Letters (1999), 462(3), 273-277  
CODEN: FEBLAL; ISSN: 0014-5793  
PUBLISHER: Elsevier Science B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A synthetic peptide (23 residues) that includes the antibacterial and lipopolysaccharide-binding regions of human lactoferricin, an antimicrobial sequence of lactoferrin, was used to study its action on cytoplasmic membrane of Escherichia coli 0111 and E. coli phospholipid vesicles. The peptide caused a depolarization of the bacterial cytoplasmic membrane, loss of the pH gradient, and a bactericidal effect on E. coli. Similarly, the binding of the peptide to liposomes dissipated previously created transmembrane elec. and pH gradients. The dramatic consequences of the transmembrane ion flux during the peptide exposure indicate that the adverse effect on bacterial cells occurs at the bacterial inner membrane.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 43 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:652824 CAPLUS  
DOCUMENT NUMBER: 132:20863  
TITLE: Cationic amphipathic peptides, derived from bovine and human lactoferrins, with antimicrobial activity against oral pathogens  
AUTHOR(S): Groenink, J.; Walgreen-Weterings, E.; van 't Hof, W.; Veerman, E. C. I.; Nieuw Amerongen, A. V.  
CORPORATE SOURCE: Section Oral Biochemistry, Department of Oral Biology, Academic Centre for Dentistry Amsterdam (ACTA), Amsterdam, 1081 BT, Neth.  
SOURCE: FEMS Microbiology Letters (1999), 179(2), 217-222  
CODEN: FMLED7; ISSN: 0378-1097  
PUBLISHER: Elsevier Science B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Peptides derived from the N-terminal domain that comprises an amphipathic  $\alpha$ -helix in human lactoferrin (LFh 18-31 and LFh 20-38) and bovine lactoferrin (LFb 17-30 and LFb 19-37) were chemically synthesized. Since many pos. charged amphipathic  $\alpha$ -helices contain antimicrobial activity, the peptides were tested for their antimicrobial activity against various oral pathogens. Both peptides from bovine lactoferrin had more potent antimicrobial activities than the human equivalent Peptide LFb 17-30, containing the largest number of pos. charged amino acids, showed the highest antimicrobial activity to both Gram-pos. and Gram-neg. bacteria. Since native lactoferrin mols. had no killing activity, release of these peptides from the native protein should be investigated to explore the use in oral care products.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 44 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 1999:262855 CAPLUS  
 DOCUMENT NUMBER: 131:97008  
 TITLE: A critical comparison of the hemolytic and fungicidal activities of cationic antimicrobial peptides  
 AUTHOR(S): Helmerhorst, Eva J.; Reijnders, Ingrid M.; van 't Hof, Wim; Veerman, Enno C. I.; Nieuw Amerongen, Arie V.  
 CORPORATE SOURCE: Department of Oral Biochemistry, Academic Centre for Dentistry Amsterdam (ACTA), Vrije Universiteit, Van der Boechorststraat 7, Amsterdam, 1081 BT, Neth.  
 SOURCE: FEBS Letters (1999), 449(2,3), 105-110  
 CODEN: FEBLAL; ISSN: 0014-5793  
 PUBLISHER: Elsevier Science B.V..  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The hemolytic and fungicidal activity of a number of cationic antimicrobial peptides was investigated. Histatins and magainins were inactive against human erythrocytes and Candida albicans cells in phosphate buffered saline, but displayed strong activity against both cell types when tested in 1 mM potassium phosphate buffer supplemented with 287 mM glucose. The HC50/IC50 ratio, indicative of the therapeutic index, was about 30 for all peptides tested. PGLa was most hemolytic (HC50=0.6 µM) and had the lowest therapeutic index (HC50/IC50=0.5). Susceptibility to hemolysis was shown to increase with storage duration of the erythrocytes and also significant differences were found between blood collected from different individuals. In this report, a sensitive assay is proposed for the testing of the hemolytic activities of cationic peptides. This assay detects subtle differences between peptides and allows the comparison between the hemolytic and fungicidal potency of cationic peptides.  
 REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 45 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:124032 CAPLUS  
 DOCUMENT NUMBER: 128:208910  
 TITLE: Cancerous metastasis inhibitors for oral administration  
 INVENTOR(S): Tsuda, Hiroyuki; Iigo, Masaaki; Tomita, Mamoru; Shimamura, Seiichi; Takatsu, Zenta; Sekine, Kazunori  
 PATENT ASSIGNEE(S): Morinaga Milk Industry Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 46 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9806424	A1	19980219	WO 1997-JP2685	19970801
W: CA, CN, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 10059864	A2	19980303	JP 1996-233652	19960815
PRIORITY APPLN. INFO.:			JP 1996-233652	A 19960815

AB The invention relates to cancerous metastasis inhibitors for oral administration which contain as the active ingredient one or more substances selected from the group consisting of iron-free saturated lactoferrin, hydrolyzates of lactoferrins, pharmaceutically acceptable derivs. of these hydrolyzates, pharmaceutically acceptable salts of these hydrolyzates, peptides originating in the hydrolyzates of lactoferrins, pharmaceutically acceptable derivs. of these peptides, and pharmaceutically acceptable salts of these peptides. These cancerous metastasis inhibitors are reduced in side effects and can be orally

administered over a long period of time, thus exerting inhibitory effects on cancerous metastasis.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 46 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:123830 CAPLUS  
DOCUMENT NUMBER: 128:235132  
TITLE: Apoptosis inducer compositions containing lactoferrin hydrolyzate peptides  
INVENTOR(S): Shimasaki, Keiichi; Watanabe, Shikiko; Azuma, Ichio; Ko, Ei Shun; Watanabe, Ryousuke  
PATENT ASSIGNEE(S): Morinaga Milk Industry Co., Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10045618	A2	19980217	JP 1996-198196	19960726
PRIORITY APPLN. INFO.:			JP 1996-198196	19960726

AB Apoptosis inducer compns. containing lactoferrin hydrolyzate peptide or its pharmaceutically acceptable salts as active ingredient are claimed. Tablets were formulated containing lactoferrin hydrolyzate peptide 50, crystalline cellulose 170, corn starch 66, talc 11 and Mg stearate 3 mg.

L11 ANSWER 47 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:782256 CAPLUS  
DOCUMENT NUMBER: 130:135788  
TITLE: Cystatin and cystatin-derived peptides have antibacterial activity against pathogen Porphyromonas gingivalis  
AUTHOR(S): Blankenvoorde, Michiel F. J.; Van't Hof, Wim; Walgreen-Weterings, Els; Van Steenberghe, T. J. Martijn; Brand, Henk S.; Veerman, Enno C. I.; Nieuw Amerongen, Arie V.  
CORPORATE SOURCE: Dep. Oral Biochemistry, Acad. Center Dentistry Amsterdam, Amsterdam, 1081 BT, Neth.  
SOURCE: Biological Chemistry (1998), 379(11), 1371-1375  
CODEN: BICHF3; ISSN: 1431-6730  
PUBLISHER: Walter de Gruyter & Co.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The authors investigated whether cystatins and cystatin-derived peptides, encompassing sequences of secondary structures of cystatin S and papain binding domains of cystatin C, display antimicrobial properties. Of the different microorganisms tested, only the growth of P. gingivalis was inhibited by chicken cystatin and cystatin C. Cystatin S, cystatin S:1-14, cystatin S:61-73 and cystatin S:108-121 also inhibited its growth, whereas cystatin S:21-38, cystatin S:39-55, cystatin S:81-95, cystatin S:94-109, and cystatin C:9-12/55-60/106-107 did not. No inhibition of the cysteine proteinase activity of P. gingivalis was observed for all cystatin-derived peptides. On the other hand, leupeptin and antipain inhibited P. gingivalis proteinase activity, but had no effect on the growth. These data suggest that cystatins contain antibacterial sequences active against P. gingivalis and that the growth inhibition does not depend on the inhibition of P. gingivalis cysteine proteinases.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 48 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:754271 CAPLUS  
 DOCUMENT NUMBER: 128:70761  
 TITLE: Parasitocides containing lactoferrins and anti-infective substances for aquatic animals  
 INVENTOR(S): Tomita, Mamoru; Hayazawa, Hironori; Kawase, Kyouzo; Yamauchi, Koji; Nakamura, Hirohiko  
 PATENT ASSIGNEE(S): Morinaga Milk Industry Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09301807	A2	19971125	JP 1996-114912	19960509
PRIORITY APPLN. INFO.:			JP 1996-114912	19960509

AB Parasitocides for cultured or aquarium fishes contain (A)  $\geq 1$  compds. chosen from lactoferrins, their hydrolyzates, peptides from the hydrolyzates, and synthetic peptides having the same amino acid sequence with the peptides and (B) anti-infective substances. A feed containing 0.005% each of lactoferrin and lactoperoxidase was fed to *Carassius carassius* to control white spot disease.

L11 ANSWER 49 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:501617 CAPLUS  
 DOCUMENT NUMBER: 127:210350  
 TITLE: Novel angiogenic disease-treating agents containing lactoferrins or their hydrolyzates  
 INVENTOR(S): Hayasawa, Hiroki; Fukuwatari, Yasuo; Shinoda, Kazumi; Nakajima, Mitsunari  
 PATENT ASSIGNEE(S): Morinaga Milk Industry Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09194388	A2	19970729	JP 1996-8722	19960122
PRIORITY APPLN. INFO.:			JP 1996-8722	19960122

AB Novel angiogenic disease-treating agents contain lactoferrins, their hydrolyzates, peptides from the hydrolyzates, synthetic peptides identical or similar to the natural peptides and/or their pharmaceutically acceptable salts as active ingredients. Tablets were formulated containing peptide from lactoferrin hydrolysis 15, crystalline cellulose 170, corn starch 66, talc 11 and Mg stearate 3 mg.

L11 ANSWER 50 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:449119 CAPLUS  
 DOCUMENT NUMBER: 127:113393  
 TITLE: Antifungal agents containing azole fungicides and lactoferrin hydrolyzates  
 INVENTOR(S): Yamaguchi, Hideyo; Abe, Shigeru; Hayasawa, Hiroki; Kawase, Kozo; Yamauchi, Koji; Wakabayashi, Hiroyuki  
 PATENT ASSIGNEE(S): Morinaga Milk Industry Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09165342	A2	19970624	JP 1995-347405	19951214
PRIORITY APPLN. INFO.:			JP 1995-347405	19951214

AB Antifungal agents contain azole fungicides and lactoferrin hydrolyzates or antimicrobial peptides derived from the hydrolyzates as active ingredients. Amino acid sequences of the antimicrobial peptides are also given. Fluconazole (I) at 1 µg/mL completely inhibited growth of *Candida albicans* TIMM 1768 in the presence of 200 µg/mL lactoferrin hydrolyzate, while 16 µg/mL was required when I was used alone.

L11 ANSWER 51 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:435756 CAPLUS

DOCUMENT NUMBER: 127:55872

TITLE: Antimicrobial peptide compositions containing fatty acid emulsions as stabilizers

INVENTOR(S): Hayasawa, Hiroki; Kawase, Kozo; Kuwata, Hidefumi; Yamauchi, Koji; Wakabayashi, Hiroyuki

PATENT ASSIGNEE(S): Morinaga Milk Industry Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.  
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09124504	A2	19970513	JP 1995-282285	19951030
PRIORITY APPLN. INFO.:			JP 1995-282285	19951030

AB Antimicrobial peptide compns. contain fatty acid emulsions as stabilizers [ peptide : fatty acid = 1 : 1 mol ratio] to prevent digestive enzyme-induced decreases in antimicrobial peptide activities. The fatty acids are selected from palmitic acid, oleic acid, linoleic acid and linolenic acid. Antimicrobial peptides are lactoferrin hydrolyzates [ e.g. Met-Arg-Arg-Trp-Gln-Trp-Arg-Met-Lys-Lys-Leu-Gly-Ala-Pro-Ser-Ile-Thr-Cys].

L11 ANSWER 52 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:264565 CAPLUS

DOCUMENT NUMBER: 126:234755

TITLE: Parasiticides containing peptides isolated from lactoferrin hydrolyzates

INVENTOR(S): Shimazaki, Keiichi; Saito, Atsushi

PATENT ASSIGNEE(S): Morinaga Milk Industry Co Ltd, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.  
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09040578	A2	19970210	JP 1995-195218	19950731
PRIORITY APPLN. INFO.:			JP 1995-195218	19950731

AB The parasiticides contain a peptide having a sequence of 31 amino acid sequences (sequence given), their pharmaceutically acceptable derivs. or salts, or mixts. of ≥2 of them as active ingredients. A peptide, i.e. Phe-Lys-Cys\*-Arg-Arg-Trp-Gln-Trp-Arg-Met-Lys-Lys-Leu-Gly-Ala-Pro-Ser-Ile-Thr-Cys\*-Val-Arg-Arg-Ala-Phe (I; 2 Cys\* residues are bonded through a disulfide bond), was isolated from a hydrolyzate obtained by hydrolysis of bovine lactoferrin with porcine pepsin. Infection rate to mouse embryonic cells of *Toxoplasma gondii* pretreated with I at 1000 µg/mL for 30 min

or  $\geq 1$  h was 16 or  $\leq 10\%$ , resp. Formulations of I, e.g. injections, ointments, were also given.

L11 ANSWER 53 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:594224 CAPLUS

DOCUMENT NUMBER: 127:275206

TITLE: Synthetic histatin analogs with broad-spectrum antimicrobial activity

AUTHOR(S): Helmerhorst, Eva J.; Van 't Hof, Wim; Veerman, Enno C. I.; Simoons-Smit, Ina; Nieuw Amerongen, Arie V.

CORPORATE SOURCE: Department of Oral Biochemistry, Vrije Universiteit, ACTA, Amsterdam, 1081 BT, Neth.

SOURCE: Biochemical Journal (1997), 326(1), 39-45

CODEN: BIJOAK; ISSN: 0264-6021

PUBLISHER: Portland Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Histatins are salivary histidine-rich cationic peptides, ranging from 7 to 38 amino acid residues in length, that exert a potent killing effect in vitro on *Candida albicans*. Starting from the C-terminal fungicidal domain of histatin 5 (residues 11-24, called dh-5) a number of substitution analogs were chemical synthesized to study the effect of amphipathicity of the peptide in helix conformation on candidacidal activity. Single substitutions in dh-5 at several positions did not have any effect on fungicidal activity. However, multi-site substituted analogs (dhvar1 and dhvar2) exhibited a 6-fold increased activity over dh-5. In addition, dhvar1 and dhvar2 inhibited the growth of the second most common yeast found in clin. isolates, *Torulopsis glabrata*, of oral- and non-oral pathogens such as *Prevotella intermedia* and *Streptococcus mutans*, and of a methicillin-resistant *Staphylococcus aureus*. In their broad-spectrum activity, dhvar1 and dhvar2 were comparable to magainins (PGLa and magainin 2), antimicrobial peptides of amphibian origin. Both the fungicidal and the hemolytic activities of dhvar1, dhvar2 and magainins increased at decreasing ionic strength.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 54 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:753870 CAPLUS

DOCUMENT NUMBER: 126:30345

TITLE: Monoclonal antibody specific to antibacterial fragment of lactoferrin

INVENTOR(S): Shimazaki, Keiichi; Saito, Atsushi

PATENT ASSIGNEE(S): Morinaga Milk Industry Co Ltd, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08269099	A2	19961015	JP 1995-73177	19950330
JP 3657644	B2	20050608		
JP 2005095185	A2	20050414	JP 2004-337304	20041122
JP 3670272	B2	20050713		

PRIORITY APPLN. INFO.: JP 1995-73177 A3 19950330

AB Monoclonal antibody specifically binds to the antibacterial fragment of lactoferrin but not the natural lactoferrin is disclosed. Eight of such antibacterial peptide fragments of lactoferrin are revealed. Sandwich immunoassay with the monoclonal antibody, enzyme-labeled antibody to specific animal Ig., plate-immobilized polyclonal antibody, and standard solution

containing similar cattle-derived lactoferrin fragment is to use for determination of

lactoferrin fragments, and ELISA anal. of the fragments were performed in e.g. stomach fluid, intestinal content, feces, blood, urine.

L11 ANSWER 55 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:268163 CAPLUS

DOCUMENT NUMBER: 124:298949

TITLE: Pharmaceutical compositions containing lactoferrin-derived peptides for treatment of cornea damage

INVENTOR(S): Sogawa, Shunji; Matsumoto, Takahiro; Yokogaki, Shuichi

PATENT ASSIGNEE(S): Senju Pharma Co, Japan; Morinaga Milk Industry Co Ltd

SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08040925	A2	19960213	JP 1994-181212	19940802
JP 3812957	B2	20060823		

PRIORITY APPLN. INFO.: JP 1994-181212 19940802

AB Pharmaceutical compns. containing lactoferrin-derived peptides are effective in treating cornea damage, especially keratitis sicca. As an example, an eye lotion contained the peptide 1, sodium chloride 0.9, sodium acetate 0.1 g, acetic acid, and sterilized purified water to 100 mL (pH 5.00). Effectiveness was tested in mice and rabbits.

L11 ANSWER 56 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:106533 CAPLUS

DOCUMENT NUMBER: 124:156014

TITLE: Topical preparations containing antifungal peptides

INVENTOR(S): Shimamura, Seiichi; Takase, Mitsunori; Yamauchi, Koji; Wakabayashi, Hiroyuki

PATENT ASSIGNEE(S): Morinaga Milk Industry Co Ltd, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07309774	A2	19951128	JP 1994-126882	19940517

PRIORITY APPLN. INFO.: JP 1994-126882 19940517

AB Topical prepsns. contain lactoferrin-related antifungal peptides (sequences given) or their pharmaceutically acceptable derivs. or salts. The peptides can be prepared by automated peptide synthesizer. An O/W-type cream contained e.g. Phe-Gln-Trp-Gln-Arg-Asn 10, Me p-hydroxybenzoate 0.1, Pr p-hydroxybenzoate 0.1, propylene glycol 12, white petrolatum 25, stearyl alc. 20, ethoxylated castor oil 4, glycerin monostearate 1, and purified water 27.8g. The prepsns. are effective in treating skin infections such as trichophytosis and showed min. side effects.

L11 ANSWER 57 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:38665 CAPLUS

DOCUMENT NUMBER: 124:97742

TITLE: Lactoferrin-related peptides as heparin-neutralizing agents and pharmaceutical compositions containing the peptides

INVENTOR(S): Kawashima, Takuji; Tomita, Mamoru; Shimamura, Seiichi; Takase, Mitsunori; Origasa, Shuzo

PATENT ASSIGNEE(S): Morinaga Milk Industry Co Ltd, Japan



SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07291874	A2	19951107	JP 1994-85143	19940422
JP 3645282	B2	20050511		

PRIORITY APPLN. INFO.: JP 1994-85143 19940422

AB Lactoferrin-related peptides (sequences given) or their pharmaceutically acceptable salts are heparin-neutralizing agents and pharmaceutical compns. containing the peptides are useful for e.g. inhibiting excessive hemorrhage due to use of antithrombotic heparin in surgery. The peptides also showed antimicrobial activities. Thus, peptide 1 and NaCl 9 mg were dissolved in 1 mL injection water and the solution was adjusted to pH 7, filtered, and distributed into an ampule.

L11 ANSWER 58 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:951321 CAPLUS

DOCUMENT NUMBER: 124:155983

TITLE: Pharmaceutical compositions containing lactoferrins or hydrolyzates and lactoperoxidase

INVENTOR(S): Yamane, Yoshihisa

PATENT ASSIGNEE(S): Morinaga Milk Industry Co Ltd, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07233086	A2	19950905	JP 1994-27049	19940224
JP 3746081	B2	20060215		

PRIORITY APPLN. INFO.: JP 1994-27049 19940224

AB Pharmaceutical compns. for treating skin disease in animals contain  $\geq 3$  weight% lactoferrins, their hydrolyzates, peptides from the hydrolyzates and/or corresponding synthetic peptides and  $\geq 3$ wt.% lactoperoxidase. As an example, lactoferrins 50 and lactoperoxidase 300g in 10L purified water were subjected to ultrafiltration for sterilization, and the resultant solution was filled into vials.

L11 ANSWER 59 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:746299 CAPLUS

DOCUMENT NUMBER: 123:138157

TITLE: Preparation and purification of antibiotic peptides from lactoferrins

INVENTOR(S): Shimamura, Seiichi; Takase, Mitsunori; Kuwata, Hidefumi

PATENT ASSIGNEE(S): Morinaga Milk Industry Co Ltd, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07145196	A2	19950606	JP 1993-156730	19930628
JP 3347819	B2	20021120		

PRIORITY APPLN. INFO.: JP 1993-156730 19930628

AB Disclosed is a method comprising (1) hydrolysis of lactoferrin and (2) purification of antibiotic peptides by membrane fractionation at pH < 5 and salt < 100 mM. In example, bovine and human lactoferrin were hydrolyzed by pig-pepsin, HCl, or V8 protease. The hydrolyzates were separated with ultrafiltration membrane module SLP-0053 (a polysulfone).

L11 ANSWER 60 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:260457 CAPLUS

DOCUMENT NUMBER: 122:101195

TITLE: A review: the active peptide of lactoferrin

AUTHOR(S): Tomita, Mamoru; Takase, Mitsunori; Bellamy, Wayne; Shimamura, Seiichi

CORPORATE SOURCE: Research and Development Laboratories, Morinaga Milk Industry Co. Ltd, Kanagawa, Japan

SOURCE: Acta Paediatrica Japonica (1994), 36(5), 585-91

CODEN: APDJBE; ISSN: 0374-5600

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review and discussion with 23 refs. presenting evidence that peptides derived from lactoferrin could potentially contribute to the host defense against microbial infections. A potent antimicrobial peptide, 'lactoferricin', was generated upon gastric pepsin cleavage of lactoferrin. The active peptide consists mainly of a loop of 18 amino acid residues, derived from the N-terminal region of the lactoferrin mol. Like various other antimicrobial peptides that display membrane-disruptive properties, it contains a high proportion of basic amino acid residues. A physiol. diverse range of micro-organisms was tested and susceptible to inhibition by this natural peptide including Gram-neg. and Gram-pos. bacteria, yeasts and filamentous fungi. Its antimicrobial effect against sensitive micro-organisms was lethal. Electron microscopy studies revealed that it induces a profound change in cell ultrastructural features and causes substantial cell damage in bacteria and fungi. These findings suggest the possibility that active peptides of lactoferrin may have a role in the host defense against microbial disease. If produced in substantial quantities in vivo such peptides could have important physiol. significance, especially in nursing infants.

L11 ANSWER 61 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:681730 CAPLUS

DOCUMENT NUMBER: 123:107583

TITLE: Antimicrobial peptides of lactoferrin

AUTHOR(S): Tomita, Mamoru; Takase, Mitsunori; Wakabayashi, Hiroyuki; Bellamy, Wayne

CORPORATE SOURCE: Nutritional Science Laboratory, Morinaga Milk Industry Co. Ltd., Zama City, 228, Japan

SOURCE: Advances in Experimental Medicine and Biology (1994), 357(Lactoferrin), 209-18

CODEN: AEMBAP; ISSN: 0065-2598

PUBLISHER: Plenum

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lactoferrin was found to contain an antimicrobial sequence near its N-terminus which appears to function by a mechanism distinct from iron chelation. Antimicrobial peptides representing this domain were isolated following pepsin cleavage of human lactoferrin and bovine lactoferrin. The antimicrobial sequence was found to consist mainly of a loop of 18 amino acid residues formed by a disulfide bond between cysteine residues 20 and 37 of human lactoferrin, or 19 and 36 of bovine lactoferrin. The identified domain contains a high proportion of basic residues, like various other antimicrobial peptides known to target microbial membranes, and it appears to be located on the surface of the folded protein allowing its interaction with surface components of microbial cells. The isolated domain, lactoferricin, was shown to have potent broad-spectrum antimicrobial properties and its effect was lethal, causing a rapid loss

of colony-forming capability. Such evidence points to the conclusion that this domain is the structural region responsible for the microbicidal properties of lactoferrin. The evidence also suggests the possibility that active peptides produced by enzymic digestion of lactoferrin may contribute to the host defense against microbial disease.

L11 ANSWER 62 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:295211 CAPLUS  
DOCUMENT NUMBER: 120:295211  
TITLE: The influence of histatin-5 fragments on the mineralization of hydroxyapatite  
AUTHOR(S): Richardson, C. F.; Johnsson, M.; Raj, P. A.; Levine, M. J.; Nancollas, G. H.  
CORPORATE SOURCE: Dep. Chem., State Univ. New York, Buffalo, NY, 14214, USA  
SOURCE: Archives of Oral Biology (1993), 38(11), 997-1002  
CODEN: AOBIAI; ISSN: 0003-9969  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The adsorption of histatin 5 on hydroxyapatite (HAP) was determined and compared to that of several fragments of histatin.5, such as residues 1-16 (N16), 7-16 (M10), 9-24 (C16), 11-24 (C14), 13-24 (C12), 15-24 (C10). The influence of the adsorbed peptides on the seeded crystal growth of HAP was investigated with the constant composition method. The adsorption affinity of the peptides as well as their ability to inhibit mineralization was influenced by the length of the peptide chain. Histatin 5 showed the highest affinity, as determined by a Langmuir model, whereas the smaller C10 and C12 displayed the lowest equilibrium uptake. The smaller C10 and C12 peptides were, on the other hand, more effective as crystal growth inhibitors, indicating a more efficient coverage of surface active sites. Electrophoretic mobility data indicated an increase in the pos. charge at the HAP surface in the presence of these peptides, which were efficient HAP crystallite dispersants.

L11 ANSWER 63 OF 63 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:449269 CAPLUS  
DOCUMENT NUMBER: 117:49269  
TITLE: Isolation of antimicrobial peptides from lactoferrin hydrolysate and their synthesis  
INVENTOR(S): Tomita, Mamoru; Kawasa, Kohzo; Takase, Mitsunori; Bellamy, Wayne Robert; Yamauchi, Kohoji Garden-haitsu; Wakabayashi, Hiroyuki Morinaga-  
PATENT ASSIGNEE(S): Morinaga Milk Industry Co., Ltd., Japan  
SOURCE: Eur. Pat. Appl., 28 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 474506	A1	19920311	EP 1991-308172	19910906
EP 474506	B1	19980513		
R: BE, CH, DE, DK, FR, GB, IT, LI, NL, SE				
JP 05092994	A2	19930416	JP 1991-186260	19910725
JP 2818056	B2	19981030		
US 5304633	A	19940419	US 1991-755161	19910905
CA 2050786	AA	19920308	CA 1991-2050786	19910906
CA 2050786	C	19981110		
AU 9183704	A1	19920312	AU 1991-83704	19910906
AU 645342	B2	19940113		
PRIORITY APPLN. INFO.:			JP 1990-238364	A 19900907
			JP 1991-186260	A 19910725

GI For diagram(s), see printed CA Issue.

AB Peptides having amino acid sequences, i.e., Lys-Cys\*-Arg-Arg-Trp-Gln-Trp-Arg-Met-Lys-Lys-Leu-Gly-Ala-Pro-Ser-Ile-Thr-Cys\*-Val or Lys-Cys\*-Phe-Gln-Trp-Gln-Arg-Asn-Met-Arg-Lys-Val-Arg-Gly-Pro-Pro-Val-Ser-Cys\*-Lle (2 Cys\* residues in each fragments are S-protected or bonded through a disulfid bond), were isolated from bovine and human lactoferrin hydrolyzates and also synthesized by an automated peptide synthesizer. Thus, a peptide (I), isolated from a hydrolyzate obtained by hydrolysis of bovine lactoferrin with porcine pepsin, in vitro inhibited 25 bacteria, e.g. Corynebacterium ammoniagenes and Staphylococcus haemolyticus with min. inhibitory concentration of 0.3 and 1 µg/mL, resp., and 7 fungi, e.g. Nannizzia incurvata with min. inhibitory concentration of 9 µg/mL. Addnl. 3 antimicrobial peptides were isolated from human and bovine lactoferrin. S-Acetamidomethylated and pyridylethylated peptides having the same amino acid sequence with I were synthesized and showed antimicrobial activity at 5 ppm. An antiperspirant spray, a tooth paste, a chewing gum containing I, etc. were formulated.

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